ACCELERATED CONDUCTION

The Wolff Parkinson White Syndrome

and Related Conditions

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This volume is from the Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California, and the Department of Medicine, University of California Medical School, Los Angeles, California.

The material was presented at McGill and University of Montreal Medical Schools as part of the 15th Louis Gross Memorial Lecture, Montreal, Canada, October 17, 1951.



FIG 1 —Single frame from high speed cinematograph of heart and simultaneously recorded electrocardiogram The electrocardiogram shows WPW beats alternating with normal beats The pen at the right has just finished inscribing a normal QRS complex The cardiac apex is seen at the top of the frame The right auricle is shown just to the left of the electrocardiogram The heart is in systole and a well developed pulmonary outflow tract is visible

MODERN MEDICAL MONOGRAPHS 3

ACCELERATED CONDUCTION

The Wolff-Parkinson-White Syndrome and Related Conditions

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GRUNE & STRATTON New York
1952

Contents

Preface

THE PROBLEM of the mechanism of Wolff Parkinson White aberration has been a topic of lively discussion for many years. Our interest in this subject grew out of certain observations made during the course of studies on the auricular arrhythmias. In examining the ventricular aberrations which sometimes occur with these arrhythmias it was seen that they often bore striking similarities to the ventricular complexes of WPW aberration. Our curiosity was further aroused when WPW complexes were observed to occur in some patients during intrathoracic operations for bronchogenic carcinoma. Moreover, in experiments in which myocardial infarction was produced in dogs by ligating the anterior descending coronary artery, it was noted that WPW complexes sometimes appeared after ligation of the artery. Here were three apparently unrelated and dissimilar situations which were capable of giving rise to ventricular aberration closely resembling the WPW type of complex, and in none did it seem possible to explain the occurrence of this aberration on the basis of any previously advanced hypothesis.

In view of these findings, and because comparatively little actual laboratory investigation of WPW aberration had been carried out, it was decided to undertake an experimental study of the mechanism of these complexes. It was soon discovered that there was no difficulty in producing the aberration in dogs by many different methods.

The most important conclusions derived from these investigation are that in both man and in the experimental animal there exist two main types of WPW aberration, a nodal type arising from a disturbance in the A V node, and a ventricular type arising from a disturbance in the ventricle proper. Of these, the nodal type appears to be more common. In three patients having the nodal type of WPW aberration significant lesions were found about and in the A V node at autopsy. In both the nodal and the ventricular types of WPW aberration the auricular impulse was found to reach the ventricles

over the normal conduction system and not by way of anomalous anatomical A-V connections. Since evidence is presented that the fundamental disorder in all types of WPW aberration is a diminution of the usual normal delay of the excitation wave at the A-V node resulting in abnormally rapid transmission of the impulse through the node, the term "accelerated conduction" has been suggested to designate this phenomenon and the aberration resulting from it. This study is the second in a series of investigations entitled "Studies on the Mechanism of Ventricular Activity."

Since previous consideration of WPW aberration had been confined largely to the classical congenital syndrome, at first it was rather a surprise when numerous acquired forms of the aberration were found to exist clinically. In fact, the incidence of acquired WPW aberration appears to be greater than that of the congenital form. It is hoped that the reader, if he watches for such cases, will also find many more clinical examples of acquired types of WPW aberration than were formerly recognized.

Because "accelerated conduction" in its various forms is not rare and because obviously much remains to be learned about this disorder, it is hoped that other observers will look for and study cases with this disturbance so that the many lacunae in our knowledge of this subject may be filled in.

For their help and cooperation in these investigations and in the preparation of this monograph, the authors wish to thank the following: Dr. Alfred Dantes, for his invaluable aid in the writing and preparation of the manuscript; Drs. John Martin Askey, John J. Sampson, John S. Lawrence, A. C. P. Bakos, A. A. Kattus, for their careful and critical reading of the manuscript; Mr. Louis Fields, for helping develop much of the apparatus used in the experiments, especially the simultaneous photography of heart and electrocardiogram; Dale Gillette, the medical photographer, whose meticulous care and skill is responsible for the electrocardiographic reproductions and the photomicrographs; Mr. Homer Alexander of Brown & Caldwell, engravers, for the color plate (Figure 1) and for Figures 26 and 27.

This study was made possible by the financial support of Morton May, Nathan Danby and Nathan Loeser (Trustees of the Louis D. Beaumont Trust Fund), Mrs. Anita May, Mr. J. Benny, Mr. H. Borun, Mr. J. M. Schmook, Mr. and Mrs. W. Goetz, Mr. E. Mannix,

Mr Adrien Pelletier Mr I Berlin, Mr L Spitz and Mr M Silberberg

We wish to express our thanks to the following authors and their respective publishers for allowing us to reproduce their illustrations Dr R Ohnell and Acta Medica Scandinavia for Figures 30A and 31A Dr M Melnick for Figure 39 and kindly loaning us Case #8 Drs H D Levine and J C Burge Jr and C V Mosby Co for Figure 41 Drs R Langendorf M Lev and R Pick for Figure 42 Drs J Gould and A S Mundal and C V Mosby Co for Figure 43 Drs S P Schwartz and A Jezer and Lea and Febiger for Figure 44 Dr W Dressler and C V Mosby Co for Figure 48 We also wish to thank the Division of Laboratories Cedars of Lebanon Hospital for the slides reproduced as Figures 38 and 40

Without the work of Eleanor Gerlach our co worker and secretary this monograph would not have been possible We also acknowledge the patience of her husband George

Dr Harry Goldblatt has not only performed an invaluable service to us by his careful study of the histology of the A V node but he has read and criticised the manuscript As Director of the Institute for Medical Research Cedars of Lebanon Hospital he has given us the utmost cooperation and guidance We extend our sincere thanks

THE AUTHORS

To Blanche

As clinical observers we study the experiments which Nature makes upon our fellow creatures These experiments however in striking contrast to those of the laboratory lack exactness possessing as they do a variability at once a despair and a delight—the despair of those who look for nothing but fixed laws in an art which is still deep in the sloughs of Empiricism the delight of those who find in it an expression of a universal law transcending even scorning the petty accuracy of test tube and balance the law that in man the measure of all things mutability variability mobility are the very marrow of his being

—WILLIAM OSLER

in his Address to the
Army Medical School Washington
February 28 1894

CHAPTER I

Introduction

THE PURPOSE of this communication is to present and interpret the results of a series of experimental investigations of the Wolff Parkinson White syndrome The interest of this laboratory in this problem was aroused when during certain investigations on ventricular aberrations occurring with auricular arrhythmias it was noticed that some of these aberrations resembled in many respects those which are commonly associated with the WPW complex[1] These similarities suggested that an experimental study of the WPW syndrome might throw new light on the problem of ventricular aberration in general especially since existing theories concerning its mechanism seem to be inadequate

An important conclusion of these investigations on the WPW syndrome was that this aberration is not dependent upon the presence of anomalous anatomical A V connections for its production and that the auricular impulses in WPW complexes are transmitted to the ventricle in an *abnormal* manner by way of the *normal conducting* system The fundamental disorder appears to consist of a *failure of a part of the A V node to delay the auricular impulse for the normal period of time before allowing its passage to the ventricles* It is suggested that the term accelerated conduction be employed to designate this condition since it describes the altered physiology more exactly than other terms

This physiologic disturbance accelerated conduction of the excitation wave through one part of the A V node instead of the normal uniform delay at the node is the fundamental disorder responsible for a number of clinical conditions The best known and most common of these is the WPW syndrome but as will be shown there are several others which result from the same basic abnormality

A thorough understanding of all the manifestations of the WPW

syndrome is necessary before the experimental portion of this study can be read

Definition

The WPW syndrome may be defined as a condition characterized by electrocardiographic and sometimes clinical abnormalities consisting of (1) variable shortening of the P R interval usually to 0 12 second or less (2) widening of the QRS complexes usually to 0 10 second or more (3) changes in the direction of the QRS complexes so that left or right axis deviation may be present (4) changes in the ST segments and T waves and (5) the frequent occurrence of paroxysmal supraventricular tachycardia and less commonly other supraventricular arrhythmias namely extrasystoles flutter and fibrillation The syndrome is observed in patients of all ages although more commonly in those below the age of 30 The male sex appears predominantly affected Usually other evidence of heart disease is lacking *but exceptions to this rule have been observed* [2] *Sudden death may* occur from paroxysms of tachycardia even in the absence of organic heart disease [3-5] but the condition is ordinarily a benign one

A large number of variations from these typical findings has been described Only those which are pertinent will be discussed here Among the unusual findings that have been reported is a P R interval exceeding 0 12 second [3,4] Rarely the P R interval in a given case may vary in duration [5] Alternation of short and normal P R intervals[6] and intermittent short P R intervals have also been observed [7]

While the common abnormality with reference to the QRS complexes is a widening to 0 10 second or more with a gradual initial slope and slurring at its onset only Ohnell[3] and Fox[8] have reported cases with short P R intervals and QRS complexes of normal width Slurring however *was present in these QRS complexes* Lown Ganong and Levine[9] have called attention to a group of patients subject to paroxysmal supraventricular tachycardia who during sinus rhythm had short P R intervals and normal QRS complexes Burch and Kimball[10] have described five types of ventricular aberration in the WPW syndrome In one of these the QRS component is not widened Slurring may affect all or any part of the QRS or may be absent altogether Abnormalities in the ST segments and T waves are frequently observed

An interesting variation from the usual form of WPW aberration is the concertina effect [3] This consists of a progressive shortening of the P R intervals with a corresponding widening of the QRS complexes in a series of WPW beats giving the impression that the complexes are being pulled out The opposite phenomenon may then be observed namely a progressive lengthening of the P R intervals and a corresponding narrowing of the QRS complexes giving the appearance of pushing in

Another variation from the typical WPW aberration and one of great importance is the frequent occurrence of A V nodal rhythm With the heart continuing to beat at a normal rate the A V node may assume the role of pacemaker spontaneously or as a result of carotid sinus pressure [11] In the many instances in which A V nodal rhythm has been observed the QRS complexes have usually been normal

In the typical case the widening of the QRS exactly compensates for the shortening of the P R interval resulting in a P J interval of normal duration Many instances have been found however in which the P J interval was shorter than the normal [1]

When the P waves of the supraventricular arrhythmias associated with the WPW syndrome can be identified they are generally inverted in leads 2 and 3 In the course of paroxysms of tachycardia previously widened QRS complexes may or may not approach the normal Wolff[13] has described two cases with very wide QRS complexes during this arrhythmia

Historical

The first comprehensive description of the syndrome was published by Wolff Parkinson and White[14] in 1930 with a review of 11 cases Prior to this there had appeared in the literature five scattered case reports with characteristic electrocardiographic findings Of these the earliest appears to have been that of Wilson[15] published in 1915 Six years later a similar case was described by Wedd [16] and in 1926 Bain and Hamilton[17] reported a third instance Two more such cases were described in 1929 [18, 19]

Interest in both the theoretical and practical aspects of the syndrome was accelerated by the paper of Wolff Parkinson and White and in the 20 years since its appearance a considerable body of literature comprising upwards of 150 papers concerning this subject has

accumulated It is not within the scope of this work to present a detailed discussion of the historical development of the syndrome excellent reviews may be found in the papers of Bishop [1] of Lepeschkin [1] and in the comprehensive monograph of Ohnell [3]

Theories Concerning The Mechanism of Production of W PW Complexes

The number and diversity of the hypotheses and suggestions which have been advanced in an effort to explain the mechanism of production of the WPW complex is remarkable Ohnell tabulated and summarized the numerous theories in existence at the time of publication of his monograph [3] and was able to include 80 papers comprising about 40 different ideas concerning this subject Furthermore since that time (1944) several additional theories have been propounded bringing the total number close to 50 Generally speaking all these theories fall into one of the following two groups

(A) Those which postulate the presence of a functioning accessory anatomical pathway by means of which the auricular impulse reaches the ventricle This concept implies that the accessory bundle is a congenital anomaly either the bundle of Kent or some other congenitally present connection between the auricles and ventricles First to suggest this hypothesis were Holzmann and Scherf and Wolferth and Wood [3] According to the theory of these investigators the auricular impulse passes over the aberrant anatomical bundle and reaches one ventricle early thus setting off a premature ventricular response and accounting for the short P R interval Shortly after this has occurred the other ventricle is activated in the normal manner This slightly asynchronous ventricular excitation is therefore responsible for the QRS aberration This hypothesis has been widely accepted

(B) A wide gamut of theories[3] postulating various bizarre and complicated abnormalities of auriculoventricular or intraventricular conduction and having in common only the concept that the impulse utilizes the normal conduction pathway None of these theories has been generally accepted

Group A The more popular theory of an accessory bundle has led to the use of the term Bundle of Kent Syndrome when referring to the WPW phenomenon

There is a considerable body of evidence in support of the thesis that potentially functional anomalous anatomical conducting pathways joining auricle and ventricle are present in some mammalian hearts Kerr and Sampson were among the earliest investigators to recall attention to the extensive microscopic studies of Kent[4] who published his first findings in 1893 Holzmann and Scherf[2] and Wolferth and Wood[3] suggested this work might afford a basis for WPW aberration Kent demonstrated the presence of a rich muscular anastomosis between auricle and ventricle in young rats and rabbits He also observed that the number of these connections decreases as the age of the animal increases or as the animal scale is ascended They are present in the monkey although relatively few in number More significantly Kent was able to show the presence of an analogous structure in the human heart a muscular bridge lying at the right cardiac border and joining the auricle and ventricle To this he gave the name of right lateral bundle and implied but did not actually state that this connection was found in all the hearts which he examined In later studies by Kent and his collaborators the essential finding of accessory muscular A V connections in animals was confirmed but no further mention was made concerning investigations on the human heart Similar muscular connections had been found as early as 1876 by Paladino [5] although his researches were by no means as comprehensive as those of Kent

A number of subsequent workers have also brought forth evidence pointing to the existence of accessory muscular A V connections Mall [6] reported their presence in both sides of the heart in embryos Monckeberg[7] described such a pathway in a greatly deformed heart studied post mortem More recently Wood and his associates [3] were able to study the heart of a 13 year old boy who during life had typical ECG findings of the WPW syndrome and died suddenly They found anatomical evidence of at least three accessory A V muscle bundles situated in the same general region as those described by Kent A left sided accessory connection was also found by Ohnell[3] in the heart of a patient with the WPW syndrome Others [9] have reported similar histologic findings The careful studies of Robb and her associates[3] have demonstrated the existence in the human embryo of such connections and have confirmed and extended the work of Mahaim[3] who showed the presence of branches connecting the main

bundle (of His) to the septum More recently Glomset and Glomset[32] have described extensive muscular A V anastomoses

Whether these accessory A V connections actually transmitted impulses remained a controversial question and no experimental approach to the problem was made until the ingenious investigation of Butterworth and Poindexter[33] These workers created an artificial aberrant A V pathway in dogs and cats by connecting one auricle to its corresponding ventricle by an electrical circuit The input derived from an electrode on the auricular surface was passed through an amplifier and fed to the surface of the ventricle or into the ventricular myocardium whereupon typical WPW complexes were produced When the direction of the current was reversed a supraventricular tachycardia resulted By introducing into the circuit a variable time delay device they were able to produce ventricular fusion beats[34] of varying type When the amplified auricular impulses were delayed a certain critical time fusion beats with WPW characteristics occurred

Ohnell[2] working with cats and monkeys produced fusion beats similar to WPW complexes by electrical stimulation near the base of the ventricles He interpreted these results as indicating transmission of impulses through anomalous A V bundles

More recently Sodi Pallares and his associates[35] were able to produce runs of WPW complexes in dogs by tapping the upper portion of the interventricular septum with a probe which had been inserted through the free wall of the right ventricle These investigators suggested that connecting aberrant bundles in the septum itself might have been responsible for these effects

This experimental evidence lends considerable support to the theory of an accessory A V pathway as an explanation of the WPW phenomenon but does not provide conclusive proof of this thesis The objective evidence in favor of contrary theories may now be briefly examined

Group B The theories embraced by this group have in common the postulation that the transmission of auricular impulses to the ventricles occurs by way of the normal channels The explanations offered for the mechanism of the production of the WPW aberration via the normal conduction system are numerous and diversified making a classification almost impossible[2, 63] No convincing objective clinical or experimental evidence has been advanced in support of any of these theories

Indirect evidence that anomalous anatomical A V pathways may not be involved in the WPW phenomenon might be adduced from the observations of Kosmann and his co workers[36] who noted that WPW complexes occurred during cardiac catheterization in two human subjects These observers offered the suggestion that the WPW aberration in these cases might be caused by the setting off of an irritable ventricular focus by the force of the inflow due to auricular contraction This hypothesis had been previously advanced by Holzmann and Scherf[7] and others[37]

The theories in this group are also supported by the fact that in many cases showing the WPW syndrome minute histologic examination of the entire A V border failed to disclose any accessory A V connections[21 ... 4]

Thus it is clear that no direct definitive demonstration of the mechanism by which WPW aberration is produced has yet been offered The experimental investigations reported in this monograph were undertaken in the hope of obtaining further objective evidence which might provide a solution to some of the questions which have been raised concerning this problem

CHAPTER II

Methods and Equipment

WPW ABERRATION was produced in dogs by a variety of stimuli applied to the A V node and to the ventricle proper A total of 144 successful experiments was achieved requiring 100 animals

The resulting phenomena were studied by electrocardiographic and cinematographic technique

Anesthesia Very satisfactory anesthesia was obtained by the use of morphine sulfate in a dose of 1 mgm per pound intramuscularly or intraperitoneally *followed by the intravenous administration* of a freshly prepared 25 per cent solution of urethane (2 cc per pound) Additional urethane was administered as necessary during the course of the experiment This combination of drugs did not cause sinus tachycardia as frequently as did the barbiturates which were employed in a previous investigation An intratracheal cannula was inserted at the start of the experiment and artificial respiration was carried on by means of a piston type automatic respirator The machine delivered 100 per cent oxygen at an average flow of about seven liters per minute

Operative Technique The operative technique for cardiac experiments developed and employed in this laboratory[1] permits wide exposure of the heart A transverse incision is made over the fourth rib from one axilla to the other The third fourth and fifth ribs are exposed and removed subperiosteally on both sides as far back as the posterior axillary line Artificial respiration is started and adjusted at this point The internal mammary vessels are ligated and divided the sternum is split transversely at the level of the fourth intercostal space The pleurae in the fourth interspace are opened bilaterally the cut ends of the sternum are widely retracted and the heart and lungs are exposed A cruciate incision is made in the pericardium The longitudinal component of this incision is made in the midline

from the diaphragmatic surface of the heart to the pericardial reflection on the aorta. The transverse component is made slightly cephalad to the point of entry of the inferior vena cava into the right auricle and extends as far dorsally as possible on the two sides of the heart cutting the phrenic nerve bilaterally at this point. The cut edges of the pericardium are stretched over the lungs and are sutured to muscles deep in the axillae; thus the auricles, the ventricles and the venae cavae are widely exposed. An intravenous infusion of normal saline solution is usually started into a femoral vein and continued throughout the experiments at a rate of one to two cubic centimeters per minute.

Cinematography. A new technique was employed to photograph heart and electrocardiographic tracing simultaneously at high camera speeds. In this way, the intimate details of the disturbed cardiac motion which occurs during WPW aberration could be correlated with the corresponding electrocardiographic events.

For this purpose it was found necessary to use an inkwriting electrocardiograph. The galvanometer and recording portion of an Edin Electrocardiograph were employed in connection with the Sanborn Polyviso amplifying system in some experiments. However, since this instrument has a paper speed of 25 mm. per second, the Brush Recorder No. *BL 202* having a paper speed of up to 125 mm. per second was used in most of these studies. This instrument can record any two leads simultaneously.

The recording electrodes for the limb leads were small hypodermic needles thrust into the limbs of the animal and connected to the electrocardiograph through small binding posts. Direct auricular and ventricular leads were obtained by means of #30 copper wire electrodes introduced into the epicardium and secured by sutures. In all unipolar lead electrocardiograms the indifferent electrode was Wilson's central terminal.

Since it is impossible for the unaided eye to analyze the details of cardiac movements occurring at their normal rates, these motions were slowed down by means of high speed cinematography. For the study of relatively gross detail of cardiac motion, color pictures were taken at a camera speed of 200 frames per second (12 x normal speed). The camera used for this purpose was a specially adapted Bell and Howell 16 mm. camera designed by Mr. Jack Bishop. For ex-

tremely detailed analysis a Western Electric Fastax 16 mm camera equipped with an F 2 3 4 inch Astro lens was used This camera can operate at speeds up to 5000 frames per second more than 300 times the normal rate Black and white films taken at high speed with this instrument were extremely valuable in studying the fine details of cardiac motions especially when it is realized that by projecting the films at half the usual rate (8 frames per second instead of 16) the motions appear twice again as slow This 600 fold reduction in speed means that if the heart is actually beating once per second each cardiac cycle on the projected film will last 10 minutes

Successful high speed cinematography depends upon the presence of intensely bright light and accurate focusing The technical details of the lighting arrangements used in these experiments need not be discussed here since they have been fully described elsewhere [1]

Photographing the movements of the heart together with the electrocardiographic tracing as it was being written presented many technical problems Since it was our desire to make an exact correlation of the cardiac movements with their electrocardiographic events it was necessary to photograph both of these on the same film and at the same time In order to simplify the study of the films it was desirable to show the heart and electrocardiograms side by side Both the tracing and heart had to be at the same distance from the camera i e in the same vertical plane or else one or the other would have been out of focus But because of the bulk of the electrocardiograph and the presence of the animal s thorax it was impossible to mount the apparatus actually beside the heart After much experimentation a simple and highly satisfactory method was developed which solved these problems and yielded the desired results This solution depended upon the use of a mirror to reflect the electrocardiographic pen and paper as the tracing was being written and the photographing of the mirror rather than the recording apparatus itself

The mirror employed was from the optical system of the periscope of an Army tank This type of mirror reflects from its front surface in contrast to ordinary mirrors thus eliminating double reflections and distortion The mirror was oblong in shape measuring approximately $1\frac{3}{4}$ inches by $3\frac{1}{2}$ inches In order to place and maintain the mirror in exactly the proper focus a specially devised stand was used The height of the mirror was adjusted by means of a rack and

pinion gear Its rotation and its angulation with reference to the electrocardiograph and camera were controlled by worm gears having a ratio of 100 to 1 These permitted very fine adjustments The height of the electrocardiograph was also adjustable by means of varying the height of an automobile jack on which it was mounted Finally the elevation of the camera could be varied so that films could be taken at any angle to the heart from the horizontal almost to the vertical The usual angle however was about 45 degrees

The electrocardiograph was placed between the camera and the heart but well below the level of the heart The mirror was placed in the plane of the camera and heart about midway between them and slightly to one side in order to avoid obstructing the camera s view of the heart By placing the mirror a few inches behind the electro cardiographic machine rather than directly above it an oblique view of the pens was obtained so that the curved tip of the pen could be clearly distinguished from the record Otherwise an appreciable period of time would have elap ed before the actual tracing became visible and correlation of cardiac movement and tracing would have been less exact The mirror was then tilted so as to reflect the surface of the electrocardiographic paper In order to place this reflection in the same focus as the heart the sum of the distances from camera to mirror and mirror to electrocardiograph must be identical with the distance between camera and heart

Since the electrocardiogram appeared inverted in the mirror (and hence in the camera) an arrangement of the circuits was made which produced inversion of the actual tracing thus yielding an upright appearance in the films

Beside the two electrocardiographic pens a time marker pen was installed in the electrocardiograph at the edge of the paper A pip every $\frac{1}{5}$ second (produced by a synchronous motor) provided a con venient time reference for the observer as well as a means of accurate calibration of the paper speed

The electrocardiographic paper was run at a speed of 125 mm per second (five times normal) and with the calibration available ac curacy was insured to 0 008 second or one small box At a paper speed of 125 mm per second and a camera speed of 5000 frames per second 40 frames are required to photograph the passage of one small box

Figure 1 (the frontis piece) shows a motion picture frame obtained

by this method The heart is at the left and the mirror image of the electrocardiogram is at the right In this instance WPW beats were alternating with normal beats The pen has just finished writing a

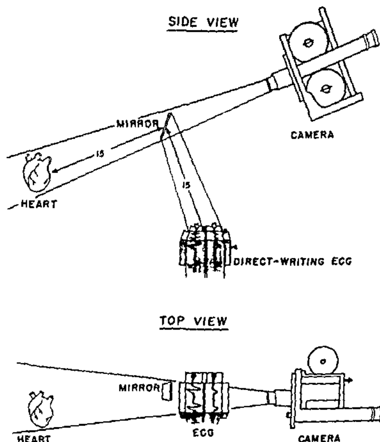


Fig 2 —Diagrammatic representation of the arrangement of equipment used for photographing together the heart and simultaneously recorded electrocardiogram Note that the electrocardiogram is filmed by photographing its reflection in a mirror placed equidistant from the heart and the surface of the electrocardiographic apparatus

normal narrow QRS complex and the heart is at the beginning of a normal systole The previous beat was a WPW beat A diagrammatic representation of the arrangements for photographing the motions of the heart and simultaneous electrocardiograph is shown in Figure 2

CHAPTER III

Experiments

Observation 1 Production of WPW Complexes by Mechanical Stimulation of the Ventricles

Mechanical Irritation of the Epicardial Surface of the Ventricles Stimulation of the epicardial surface of the ventricle was effected in the exposed heart of the dog by stroking with a wooden applicator This method of irritation usually produced ventricular premature beats or runs of ventricular tachycardia By careful manipulation however short episodes of WPW aberration were obtained at frequent intervals in almost every animal studied Long runs of these complexes however were not achieved by this method The stimulating applicator was always applied at a distance from the A V groove This was done in order to avoid stimulating any possible anomalous anatomical A V connections

This procedure was successful in producing WPW patterns on 17 occasions when applied to the right ventricle (Figure 3A) and on 17 occasions when applied to the left ventricle (Figure 3B) In each of several dogs ventricular complexes of different types were produced by stimulation of different areas of the ventricles

Mechanical Irritation of the Endocardial Surface of the Ventricles In three experiments a purse string suture was placed in the wall of the right auricular appendix A small incision was then made within the suture and a metal rod was passed through the opening The suture was then pulled tightly enough to prevent the escape of blood and the rod was advanced through the tricuspid valve into the right ventricle

Pressure by the tip of the rod exerted on either the septum or on the free wall of the right ventricular cavity produced isolated WPW complexes and also runs of alternating normal and WPW complexes (Figure 3C) On one occasion the tip of the rod was held firmly against

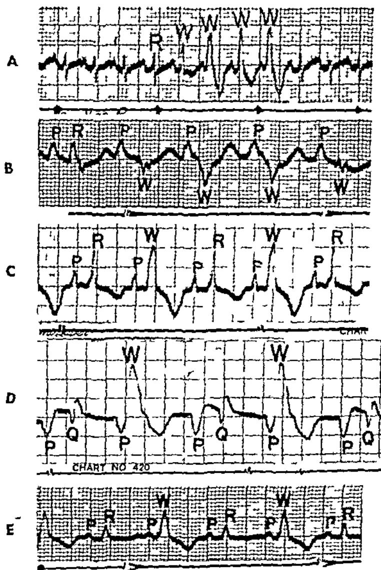


Fig 3—Electrocardiograms showing WPW complexes produced in dogs by mechanical stimulation of various portions of the ventricles In each tracing the WPW beats are indicated by W

(A) Mechanical stimulation of epicardium of right ventricle Lead AVF

(Continued on page 15)

the endocardial surface of the anterior wall of the right ventricle about midway between the apex and the base and about 1½ inches from the septum Pressure with the rod was maintained for approximately 7½ minutes Throughout this entire period a run of alternating WPW and normal complexes was recorded

Five similar experiments were carried out relative to the left ventricle In each of these WPW aberration was produced by stimulating the endocardial surface of this cavity (Figure 3D)

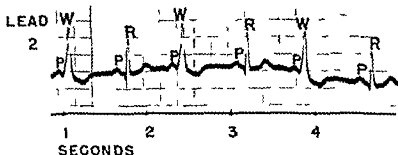


FIG 4 —Electrocardiogram of a patient showing a run of WPW complexes alternating with normal complexes Note similarity to Fig 3 C and E when the same phenomenon was observed in the dog by mechanical stimulation

Production of WPW aberration by mechanical stimulation of the ventricles as described above is simple and results in a high proportion of WPW complexes The experiment is easily reproducible since it requires no elaborate or sensitive apparatus for producing the proper stimulus Because ventricular extrasystoles and tachycardia often occurred in addition to the WPW aberration it was necessary to determine whether the latter was the result of chance A statistical analysis demonstrating that this was not the case will be found in the Appendix

It should be noted that during experimental cardiac catheterization

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(Continued from page 14)

(B) Stimulation of epicardium of left ventricle Lead 3

(C) Endocardial stimulation of right ventricle Direct auricular lead

(D) Endocardial stimulation of left ventricle Direct auricular lead

(E) Endocardial stimulation of right septum Lead 3

Note in tracing C and E the WPW complexes alternate with normal complexes

in dog W P W complexes have been observed undoubtedly as a result of endocardial stimulation by the catheter

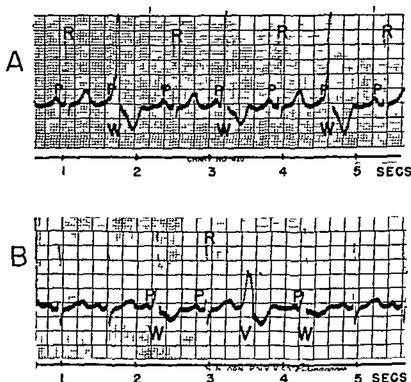


Fig 5—(A) W P W complexes occurring in a patient during cardiac catheterization

(B) The appearance of ventricular extrasystoles in addition to W P W complexes in the same patient during cardiac catheterization

The alternating type of W P W aberration which has been noted in these experiments has also been observed to occur clinically (Figure 4) *Instances in which this phenomenon has occurred have been reported* by Cain[6] who maintains that alternation of this kind is present in as many as 10 per cent of all patients with the W P W syndrome

Cardiac catheterization in man The occurrence of W P W complexes in human subjects undergoing intracardiac catheterization has been noted by Kossmann et al[46] This observation has been confirmed in

this laboratory investigation by reviewing a large number of clinical records taken during cardiac catheterization. A high percentage of WPW complexes was found to occur during the procedure (Figure 5A). The mechanical stimulus provided by the presence of the catheter within the right ventricular cavity appears to have been responsible for the production of the WPW phenomenon. Figure 5B demonstrates that ventricular premature beats are also of frequent occurrence during cardiac catheterization in man. Their high incidence again made a statistical analysis necessary (Appendix).

WPW aberration was produced by mechanical stimulation of either ventricle. Successful results were obtained from both epicardial and endocardial stimulation. In all instances the stimulus was applied to areas far from the A-V groove, thus avoiding any possible anomalous A-V connections. By this method isolated WPW complexes, short runs of WPW aberration and runs of WPW complexes alternating with normal complexes were produced. The latter type of aberration is not unusual in the clinical syndrome. WPW aberration was also seen to occur in man during cardiac catheterization, a form of mechanical stimulation of the endocardial surface of the ventricle.

Observation 2. Production of WPW Complexes by Chemical Stimulation of the Ventricles

For this purpose 0.05 per cent aconitine in benzene was found most suitable (Figure 6). This dilution was necessary since application of stronger solutions usually produced ventricular extrasystoles, tachycardia or fibrillation. With this technique WPW aberration was produced nine times by stimulating the right ventricle and seven times by stimulating the left ventricle. Again the direction of the major deflection of the QRS complexes varied with the site of application of the stimulus.

In these experiments many of the electrocardiographic features of the WPW syndrome were reproduced. In general, however, this method of producing WPW aberration is not as satisfactory as the mechanical. Even the most meticulous preparation and application of the solution did not always prevent the occurrence of the undesired *arrhythmias already mentioned.* Nevertheless, when ventricular

tachycardia appeared it was sometimes still possible to produce WPW complexes by cooling the stimulated area by means of an ethyl chloride spray It is of interest that when runs of ventricular tachycardia occurred they were usually initiated by WPW complexes (Figure 7)

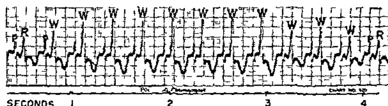


FIG 6—Direct auricular lead from a dog showing a run of WPW complexes illustrating the concertina effect produced by the application of aconitine to the epicardial surface of the right ventricle

A statistical analysis of the results of chemical stimulation of the ventricles showing that the production of WPW complexes by these methods was not due to chance will be found in the Appendix

Chemical stimulation of the epicardial surface of the ventricles in regions far removed from the A V groove produced many of the electrocardiographic features of the WPW syndrome This method of producing WPW aberration however is not as satisfactory as mechanical stimulation

Observation 3 The Role of the Ventricular Inflow Tract

Holzmann and Scherf[30] as well as a number of later investigators[59] have advanced the theory that the WPW aberration is due to an irritable ventricular focus which discharges prematurely when the auricles eject blood forcibly into the ventricles This hypothesis was investigated in the following manner

1 *Left Inflow Tract* We have seen in high speed cinematographs that the body of the left auricle of the dog is non contractile[1] The left inflow tract therefore normally is weak The contractile left auricular appendix was ligated near the base thus eliminating or markedly reducing the effect of auricular contraction *Despite this* procedure it was possible in 2 instances to produce WPW complexes

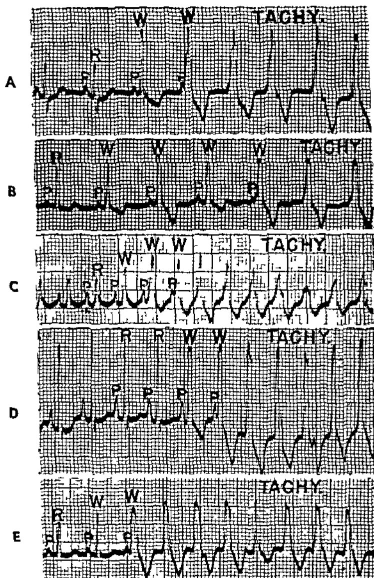


Fig 7 — Examples of paroxysms of ventricular tachycardia produced in dogs by the application of aconitine to the ventricle Each paroxysm is initiated by WPW beats Lead AVF

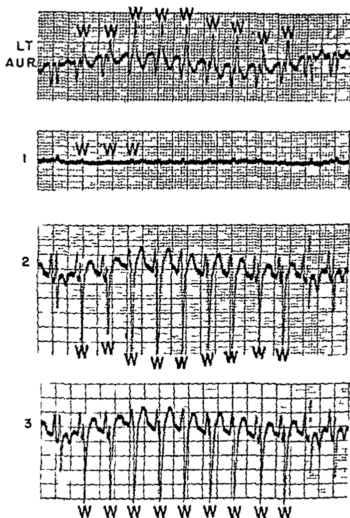


Fig. 8.—Four simultaneous leads from a dog showing the production of WPW complexes by chemical stimulation of the ventricle after elimination of the effect of left auricular contraction by ligation of the left auricular appendix. In the dog the body of the left auricle is non contractile. The force of inflow to the left ventricle can therefore be markedly reduced by ligating the contractile left auricular appendix. Since WPW complexes can still be produced after this procedure it would seem unlikely that the force of inflow resulting from auricular systole and acting on a ventricular focus could be responsible for their occurrence.

by the *application* of aconitine to the left ventricle as described above (Figure 8)

2 *Right Inflow Tract* The inflow tract of the right ventricle was reduced to insignificant proportions by clamping the superior and







...mmediately after virtual ...ntricle by clamping both ...compression of the v nae

...t of this nature which ...immediately after the

In view of the phenomena it cannot be maintained that the mechanical force of that portion of the inflow tracts in the ventricle

produced by auricular contraction is a requisite factor which sets off a premature discharge of a hyperirritable ventricular focus to produce the WPW complex Additional evidence in opposition to this theory may be adduced from clinical experience since in conditions such as hyperthyroidism or during exercise when the cardiac inflow is markedly increased WPW aberration does not generally occur Actually exercise often will abolish the aberration On the other hand WPW aberration is not known to disappear in patients with WPW who develop a weak cardiac inflow as in shock

Virtual elimination of that portion of the inflow to either side of the heart due to auricular systole failed to prevent the occurrence of WPW complexes The force of the blood flow into the ventricles which results from auricular systole therefore cannot be a factor in initiating these complexes

Observation 4 Production of WPW Aberration by Stimulation of the Ventricles with Direct Electrical Current

The methods used in Observations 1 and 2 (mechanical and chemical stimulation of the ventricles) for the production of WPW complexes although successful in a significant number of instances are not entirely satisfactory Ventricular extrasystoles and tachycardia occurred so frequently that it was necessary to make a statistical analysis in order to prove that the WPW complexes were more than chance events

It was thought therefore that a method of stimulating by means of a non interrupted direct electrical current would prove successful Direct current was consequently obtained from either the rectified and filtered power supply for a thyratron stimulator or from B batteries Through the use of power rheostats a system was devised by which both the voltage and amperage of the direct current delivered to the animal could be varied Most commonly the intensity of the current used in our experiments was 0 25 to 1 5 milliamperes with a potential of 15 to 75 volts

The stimulating electrode used for epicardial application was a *fine (#30)* copper wire which was stitched into the epicardium For stimulating endocardially a heavier insulated copper wire was used

To the end of this was attached a small ball of solder wrapped in cotton which had been soaked in saline solution In all experiments the stimulating electrode was cathodal The anodal electrode was a small hypodermic needle thrust into the right hind limb of the animal and connected to the power supply through a small binding post With this equipment if the anodal electrode was applied at other areas troublesome electrical interference was noted in the electrocardiograms Numerous areas on either the epicardial or endocardial surfaces of the right or left ventricle were stimulated

In order to stimulate the endocardial surface of the ventricles the stimulating electrode was introduced into either the right or left auricle through a small incision which was then closed by a previously placed purse string suture The electrode was passed through the auriculoventricular valve until its tip was in contact with the endocardial surface of the ventricle With practice it was possible to determine quite accurately the location of the electrode within the ventricular cavity and to maintain its position throughout the experiment When the electrode had been placed at the desired spot the current was turned on and gradually increased while electrocardiographic tracings were recorded

A total of 37 successful experiments was performed using continuous current as a stimulus By trial a current of *subthreshold intensity* was found and used to produce WPW aberration This current was not of sufficient magnitude to set off ventricular contractions but was capable of altering the area stimulated in such a way that the normal excitation impulses produced the abnormal premature ventricular response

WPW aberration of all clinical types was produced whether the stimulus was applied epicardially or endocardially and with frequent success from stimulating either ventricle The most consistently satisfactory results however were obtained by stimulating the endocardial surface of the right ventricle at or near the apex As in the previous experiments if the stimulus was too great ventricular extrasystoles appeared and when the strength of the current was increased further ventricular tachycardia often occurred On rare occasions in dogs with hyperirritable ventricles it was not possible to produce WPW aberration a high incidence of ventricular tachycardia resulted instead In general however the abnormalities

occurred so much less frequently than with mechanical or chemical stimulation that it was unnecessary to make a statistical analysis as in Observation 1 and 2

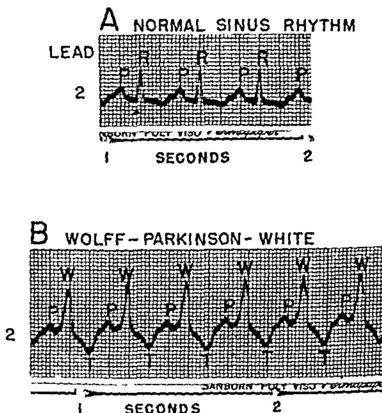


Fig. 10 —(A) Normal sinus rhythm in a dog
(B) Continuous WPW aberration in the same animal produced by uninterrupted subthreshold electrical stimulation of the endocardial surface of the right ventricle high on the intraventricular septum

The various forms of WPW aberration produced in this experiment may be classified as follows

I *Continuous WPW aberration* Figure 10 shows an example of this type of aberration resulting from endocardial stimulation of the right ventricle high on the interventricular septum

II *WPW complexes alternating with normal complexes* This alternation was maintained for as long a period as the stimulation was continued Figure 11A shows continuous WPW complexes while Figure 11B demonstrates alternating WPW and normal complexes produced in the same animal

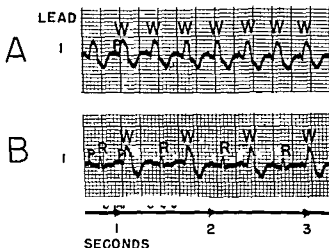


FIG 11 —(A) Continuous WPW aberration in a dog produced by uninterrupted subthreshold electrical stimulation of the endocardial surface of the right ventricle at the apex

(B) WPW complexes alternating with normal complexes in the same animal and produced in the same manner as in (A)

III *The phenomenon which Ohnell (3a) has called the concertina effect* Figure 12A shows this effect produced experimentally in the dog and Figure 12B shows its occurrence in man This phenomenon occurs experimentally without changing the intensity of the stimulating current

It was impossible to predict which one of these three forms of WPW aberration would result when stimulating a given area of the ventricle An adequate explanation for the appearance of these variations which occurred under the same experimental conditions is not readily apparent

IV *Variations in the configuration of WPW complexes* A number

of differently shaped WPW complexes were produced their configuration depended upon the area of the ventricle stimulated These

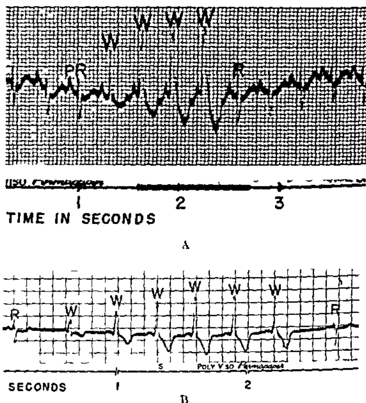
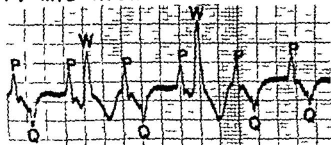
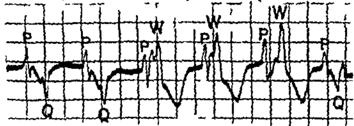


Fig 12—(A) A run of WPW complexes in a dog showing the concertina effect produced by uninterrupted subthreshold electrical stimulation of the pericardial surface of the right ventricle near the base of the pulmonary conus Lead 3

(B) A run of WPW complexes in a patient showing the concertina effect Lead 3 Note similarity to (A)

changes are well seen in Figure 13 which shows the effect upon the form of WPW aberration of changing the site of stimulation It was observed that when the stimulus was applied on the epicardial surface directly over the septum the QRS complexes were often very narrow





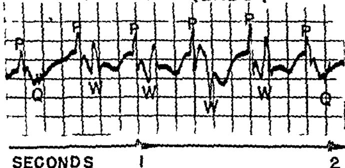


Fig 13 —Left auricular lead from a dog showing the production of WPW complexes by stimulating various sites of the right ventricle by uninterrupted subthreshold electrical current. Note that the shape of the ventricular component of the WPW complexes varies with changes in the site of stimulation

Figure 14 shows a complex occurring during stimulation at the left

An observation of considerable clinical interest was the occasional production of WPW complexes showing only slight changes in the P R interval and QRS complex. This usually occurred when a weak current was used. This minor aberration was seen best in the direct

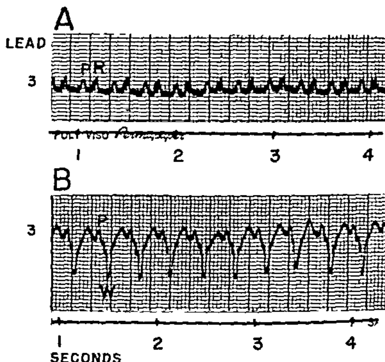


FIG. 14.—(A) Normal sinus rhythm in a dog.
(B) Continuous WPW aberration in the same dog produced by stimulation of the epicardial surface of the apex of the left ventricle by uninterrupted subthreshold electrical current. Note the marked inversion of the QRS complexes.

auricular and ventricular leads. In limb leads these minor aberrations were manifested by slightly increased or decreased amplitude of the R waves and minor changes in the T waves. Aberrations of this type may be seen in the 3rd complex of Figure 7A and in the 3rd, 4th and 5th complexes of lead AVF in Figure 7B. Although abnormalities in these complexes are slight, it is nevertheless evident that they represent a form of WPW aberration since they usually precede or

follow runs of well marked WPW complexes At other times continuous minor aberrations occurred recognizable only when the current was turned off and the tracing compared to the normal record then being registered The clinical significance of these minor aberrations will be discussed later

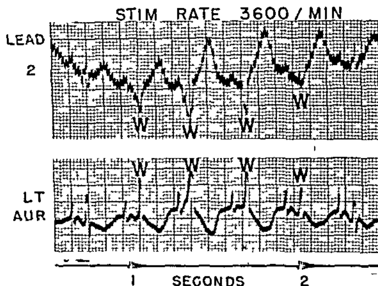


Fig 15 —Simultaneous tracings showing the production of WPW aberration in a dog by interrupted subthreshold electrical stimulation of the body of the left ventricle The fine deflections in lead 2 are due to the stimulating current itself The rate of stimulation is 3600 impulses per minute

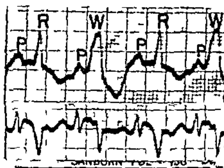
Increasing the strength of the stimulating current to 2 to 3 milliamperes and 80 to 125 volts produced runs of WPW complexes but these were generally superseded by ventricular tachycardia In some instances however it was possible to produce single WPW complexes with a strong current

In a few experiments short runs of WPW aberration were produced by an *interrupted* direct current applied to the epicardial surface of either ventricle (Figure 15) Interrupted stimulation was delivered to the epicardium through a conventional thyratron pulse generator

A

Auric Rate—200/min
Lead 2

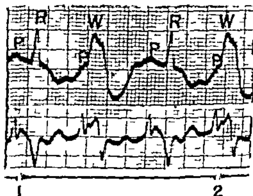
Direct Auric lead



B

Auric Rate—176/min
Lead 2

Direct Auric lead



C

Auric Rate—230/min
Lead 2

Direct Auric lead

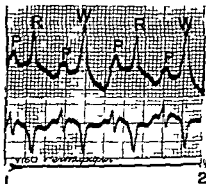


Fig. 16 —Simultaneous leads from a dog showing a run of alternating WPW aberration produced by endocardial stimulation of the upper portion of the right side of the septum by subthreshold uninterrupted electrical current (A)

(Continued on page 31)

having an adjustable voltage output and capable of delivering stimuli at rates variable from 75 to 4000 per minute Adventitious deflections in the tracings were often noted with this method due to the stimulating current itself

The method of choice for the production of WPW aberration is by the use of continuous direct electrical current since (1) all the known clinical types could be produced—isolated WPW beats continuous WPW aberration alternating WPW and normal beats the concertina effect and minor forms of WPW aberration hardly detectable by limb leads and picked up mainly by direct cardiac leads (2) little distortion was introduced into the tracings by the stimulating current and (3) the aberration could be produced more consistently than with other methods Nevertheless ventricular extrasystoles and tachycardia did occur as undesirable effects of this method of stimulation

Effect of Changing Heart Rate In the foregoing experiments the possibility exists that the aberration produced might be a manifestation of idioventricular rhythm or ventricular tachycardia rather than WPW aberration If an idioventricular rhythm happened to give rise to premature beats at a rate which exactly corresponded to the auricular rate it would be difficult to differentiate the resulting complexes from those of WPW aberration

In order to investigate this possibility some of the experiments were repeated When typical WPW complexes were produced as a result of electrical stimulation the heart rate was increased or decreased by heating or cooling the S A node This was most simply done by applying a test tube containing either hot or cold water to the region of the node Figure 16 demonstrates alternating WPW and normal complexes produced by stimulation of the upper portion of the septal endocardium It should be noted that despite the changes in auricular rate produced by varying the temperature of the S A node each aberrant QRS complex is preceded by a P wave In Figure 16B where the P waves in lead 2 are partly buried in the abnormal ventricular complexes the simultaneous direct auricular lead demon

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(Continued from page 30)

The aberrant ventricular complexes continue to follow the P waves although the auricular rate has been decreased from 200 to 176 by cooling the S A node (B) and increased to 230 by heating the S A node (C) This indicates that the auricles and not the subthreshold current are driving the ventricles

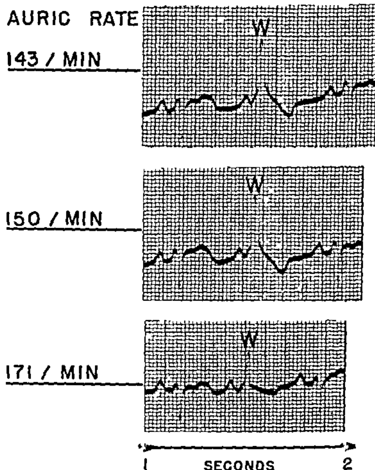


FIG 1 —Lead 3 showing that the aberrant ventricular complexes continue to follow P waves although the auricular rate has been varied by heating and cooling the S A node

strates them clearly Figure 17 showing single WPW complexes produced by stimulating in the mid septal region again demonstrates the abnormal ventricular complex following the auricular complex even though the auricular rate has been varied This consistent relationship between auricle and ventricle in the presence of changing auricular rates shows clearly that the ventricles in these experiments

were being driven by the auricles and excludes idioventricular rhythm or ventricular tachycardia

Stimulation of the ventricles by means of non interrupted direct electrical current was found to be an excellent method for producing W P W aberration Although ventricular extrasystoles and tachycardia sometimes occurred this method of stimulation was preferable to the mechanical and chemical methods used in Observations 1 and 2 With the use of continuous current stimulation all of the known clinical types of W P W phenomena were produced including isolated W P W beats constant W P W aberration alternating W P W complexes the concertina effect and minor abnormalities detected best by direct leads from the surface of the heart The shape of the QRS deflection varied with the area stimulated

Observation 5 Production of WPW Complexes by Stimulation of the A V Node with Noninterrupted Direct Electrical Current

In all the previous experiments WPW aberration was produced by stimulating various areas of the ventricles Translated into terms of the human WPW syndrome these results would indicate that the aberration has its origin in a ventricular focus Yet if this were the case one would expect patients with this condition to exhibit other evidence of an irritable ventricular focus such as ventricular extrasystoles and possibly tachycardia However these phenomena are rarely observed in patients with the WPW syndrome Therefore it seems unlikely that most instances of the clinical aberration can be associated with a ventricular focus

On the other hand extrasystoles arising in or near the A V node are frequently seen in patients with the WPW syndrome (Figure 18) In the esophageal lead of this tracing the retrograde P wave indicates that the impulse originates at the A V node Furthermore the paroxysmal tachycardia which is common in this condition and the flutter which is occasionally observed are thought to be nodal in origin Cases of this kind have been reported by Rosenbaum et al [11] Wolff [13] Wolff and White [12] and by Ferrer and her associates [33] The nodal origin of these arrhythmias is suggested by the presence of

inverted and retrograde P waves In some instances e ophag leads may be required in order to demonstrate their true nature

It was decided to determine experimentally whether WPW ab ration could be produced by stimulating the A V node in the sa manner in which the ventricles had been stimulated as described Observation 4

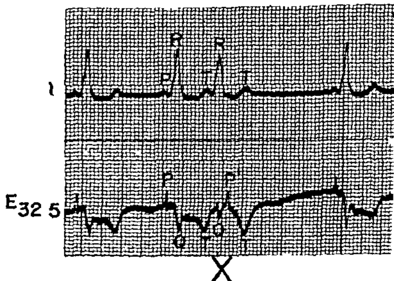


FIG 18 —Simultaneous tracings of Lead 1 and an esophageal lead at a dep of 32 5 centimeters in a patient with WPW aberration At the point X the occurs an extrasystole In the esophageal lead it is clear that the P wave fo lows the Q wave in this beat thus strongly suggesting that the extrasysto is nodal in origin

Locating the A V node was accomplished in the following manne The stimulating electrode was introduced into the right auric through a pur e-string opening at the appendix and advancing it the level of the coronary sinus The position of the electrode with the auricle could be determined by palpating its tip through th auricular wall The region of the coronary sinus was explored b stimulating various areas on the caudal surface of the auricle wit interrupted current With each area stimulated simultaneous electr cardiograms were recorded When the A V node was touched

shortened P R interval was observed (Figure 19), and inversion of the P waves occurred in leads 2 and 3 In one experiment it was noted that as the stimulating electrode was applied to successively more caudad regions of the node the P P interval became progressively shorter (Figure 20) Definite proof that the node had been located was obtained if too much pressure was exerted on the stimulated area with the tip of the electrode for then complete heart block appeared (Figure 21) When the pressure was relaxed the block disappeared The electrode was then maintained in this position the

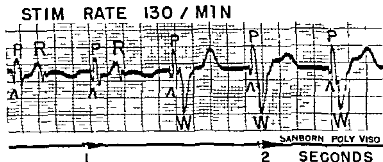
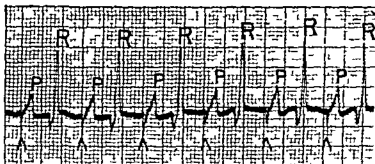


FIG 19—Direct auricular lead from a dog showing WPW complexes produced by stimulating the region of the A V node with an interrupted electrical current of greater than threshold intensity The instant of application of the current is indicated by an inverted V The first two complexes are normal and occurred when the tip of the electrode was approaching the A V node When the electrode was moved further caudad WPW complexes occurred as in the 3rd and subsequent beats in this tracing Note that the P R interval becomes very short and the QRS complexes aberrant

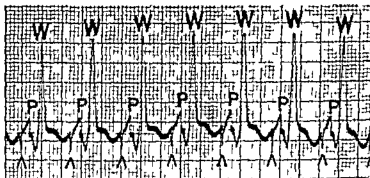
current was changed to the continuous type and attempts were made to produce WPW aberration

In 17 experiments in which the node was successfully located it was possible to produce WPW complexes in 7 instances (Figures 22 and 23) The current used in these experiments was of subthreshold intensity and therefore could not have been driving the ventricles This was confirmed in one experiment in which the auricular rate was purposely varied by heating the S A node as in Observation 4 it was then seen that the ventricular portion of the WPW complexes continued to follow the auricular waves at the increased rate With the

A



B



C

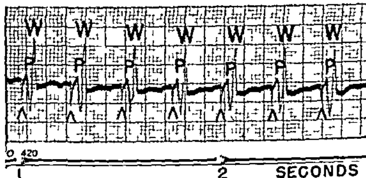
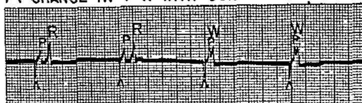


Fig 20.—(A) Normal complexes produced by stimulating the endocardial surface of the right auricle of a dog at a distance from the A V node using an interrupted electrical current of greater than threshold intensity The sharp downward deflections indicated by the inverted V s are due to the stimulus itself Note that the P R intervals are normal

(B) The stimulating electrode has now been moved to the A V node and WPW complexes with short P R intervals have appeared

(C) The stimulating electrode has now been moved to a more caudal area of the A V node WPW complexes with still shorter P R intervals have resulted

non-interrupted current stimulating the A-V node the P waves in the WPW complexes were always normal and in no instance did ventricular extrasystoles or tachycardia occur Thus the results obtained



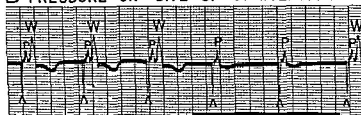


FIG 21 —(A) Shortening of the P-R interval and the occurrence of WPW complexes in a dog as the stimulating electrode is moved toward the A-V node Interrupted electrical current of greater than threshold intensity

(B) When increased pressure is exerted on the site of stimulation by the electrode complete heart block occurs proving that the electrode is actually on the A-V node The first 3 beats are WPW complexes produced as in (A) During the 4th and 5th beats strong pressure is being exerted on the A-V node and QRS complexes fail to appear after P waves At the 6th beat this pressure is relaxed and WPW complexes reappear This demonstrates that WPW beats and high grade A-V heart block can exist in the same tracing

by this method more closely simulated the characteristics of the clinical syndrome than did stimulation of the ventricles in which extrasystoles and tachycardia frequently occurred in addition to WPW aberration

While locating the A V node with interrupted current WPW complexes often occurred When the current was turned off post stimulatory WPW complexes occasionally persisted

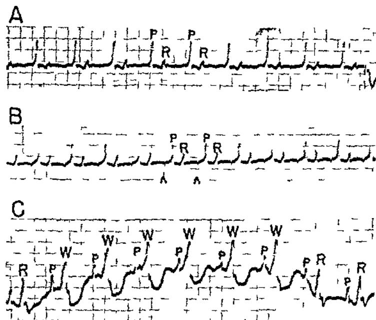


FIG 22—(A) Normal sinus rhythm in a dog before application of stimulus Left auricular lead

(B) Stimulation of A V node of same dog with interrupted electrical current of greater than threshold intensity Note that the P R interval has become shorter

(C) Stimulation of same point in A V node now using uninterrupted subthreshold electrical current resulting in WPW aberration Note concertina effect

The A V node may be located by applying an interrupted electrical current to the region of the node, and noting when the P R interval becomes shortened and P wave inversions occur in leads 2 and 3

Confirmation can be obtained by the occurrence of complete heart block when excessive pressure is exerted on the node When the current was changed to non interrupted and was of subthreshold intensity WPW aberration resulted However no ventricular extrasystoles or

tachycardia resulted from nodal stimulation in contrast to their frequent appearance with ventricular stimulation Thus the clinical picture was more closely reproduced with nodal than with ventricular stimulation

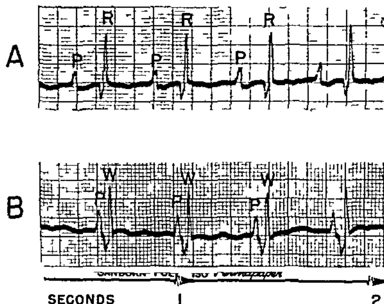


FIG 23 —(A) Normal sinus rhythm in a dog Left auricular lead
(B) WPW aberration produced in the same animal by stimulating the A V node with uninterrupted subthreshold electrical current Left auricular lead The QRS complexes are normal in width and configuration but the P R intervals are very short

Observation 6 Production of Tachycardia and Other Arrhythmias Occurring in the WPW Syndrome by Stimulation of the A V Node with Interrupted Direct Electrical Current

Four types of supraventricular arrhythmias occur in the WPW syndrome Of these tachycardia is the most common but nodal extrasystoles flutter and fibrillation may also be observed Any theory which attempts to explain the WPW syndrome must therefore be able to explain the mechanism of how all these arrhythmias occur

The widely accepted theory of aberrant anatomical A V bundles offers an explanation for the occurrence of paroxysmal auricular tachycardia According to this theory tachycardia results from retrograde conduction of impulses from ventricle to auricle with a 1 1 ventriculo-auricular rhythm However it does not explain the occurrence of auricular flutter in which A V block is almost invariably present in some degree If A V block is present it is obvious that the ventricular rate is slower than that of the auricles and cannot be driving them Even in the absence of block this theory would fail because a ventricular rate of about 300 per minute would be required to produce auricular flutter Nor can auricular fibrillation be explained by the theory of aberrant anatomical bundles for it is known that the stimulatory rate required to produce auricular fibrillation in man may be as high as 300–400 impulses per minute[1] The accessory bundle theory would again demand a ventricular rate of at least 300 per minute in order to initiate fibrillation of the auricles Such rapid ventricular rates however are impossible Thus it is seen that the theory of aberrant anatomical bundles while offering an explanation for the auricular tachycardia fails to account for the mechanism of how auricular flutter and fibrillation occur in the WPW syndrome

Is there then any single theory capable of explaining all four of the auricular arrhythmias which may occur in the syndrome? A strong suggestion in favor of this possibility is contained in the realization that the extrasystoles the tachycardia and the flutter occurring in the clinical WPW syndrome all arise at or near the A V node The origin of the fibrillation cannot be determined by examining the electrocardiogram

Therefore an experiment was conducted to determine what would occur if the altered area in the node responsible for the appearance of WPW complexes were made the *pacemaker* Specifically an attempt was made to discover whether it would be possible in this way to produce all the auricular arrhythmias of the WPW syndrome

In six experiments the A V node was located in the manner described in Observation 5 The node was then stimulated with interrupted current at increasingly rapid rates

It was found that with a relatively slow stimulatory rate extrasystoles occurred When the rate was increased tachycardia resulted (Figure 24B) In each instance the P waves were inverted in leads

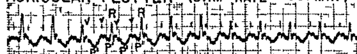
NORMAL SINUS RHYTHM



AURICULAR TACHYCARDIA (STIM RATE 250)



AURICULAR FLUTTER (STIM RATE 500/MIN)



AURICULAR FIBRILLATION (STIM RATE 750)



POST-STIMULATORY FIBRILLATION



FIG 24 —The uppermost tracing shows normal sinus rhythm in a dog before stimulating the A V node The subsequent tracings demonstrate the production of auricular tachycardia auricular flutter and auricular fibrillation in the same animal by progressively increasing the rate of stimulation of the same point in the A V node using interrupted electrical current of greater than threshold intensity The lowermost tracing was made after the current was turned off but fibrillation persists This experiment demonstrates that auricular arrhythmias *can result when the same area in the A V node* which was responsible for W P W aberration (as in figure [illegible]) is made to function as the pacemaker at various rates of discharge

2 and 3 When still faster stimulatory rates were used auricular flutter was produced (Figure 24C) and with a further increase in rate of stimulation auricular fibrillation ensued (Figure 24D) On several occasions post stimulatory auricular fibrillation was observed (Figure 24E)

These findings are in accord with the theory of the unitary nature of the auricular arrhythmias[1] In previous investigations from this laboratory it was shown that the critical factor which determines which one of these arrhythmias will occur is the rate of discharge of the A V node which acts as the ectopic focus If both the S A node and the A V node are discharging at rates of 100 and 75 respectively only occasional extrasystoles can be produced from the A V node since most of its impulses will be meeting refractory tissue If however the rate of discharge of the A V node increases to 150 while the S A node continues at 100 the A V node becomes the pacemaker and nodal tachycardia will result Now all the impulses from the S A node will meet refractory tissue In the event that the A V node discharges still faster for example at a rate of 300 auricular flutter will usually occur and at a rate of 400 auricular fibrillation will ensue

In the present series of experiments all the auricular arrhythmias observed in the clinical WPW syndrome have been reproduced These arrhythmias arose from a region of the auricle at or near the node It is thus shown experimentally that when the altered area in the node which ordinarily gives rise to WPW complexes (Observation 5) becomes the pacemaker arrhythmias appear Merely increasing the rate of stimulation of the node results in the production of extrasystoles tachycardia flutter and fibrillation in turn

Thus in the light of the observation that an altered area in the A V node is responsible for the occurrence of WPW complexes and that when the same area becomes the pacemaker all the supraventricular arrhythmias of the WPW syndrome can be produced an explanation for the entire clinical picture is provided It has been seen that the theory of aberrant anatomical bundles cannot account for all the manifestations of the syndrome since neither auricular flutter nor fibrillation can be explained on such a basis For this and other reasons to be presented later it would appear that this theory is not completely satisfactory

The concept developed in the present study is that a portion of the

node is altered in such a way that it allows premature conduction of the auricular impulse to a part of one ventricle While this is taking place the unaltered portion of the node delays the remainder of the impulse in the normal manner and then transmits it to the rest of the ventricles The basis for this theory will be shown in the next section

Any theory attempting to explain the mechanism of the W P W syndrome must be able to explain all of its manifestations The theory of aberrant anatomical bundles (bundle of Kent etc) cannot explain the occurrence of all the supraventricular arrhythmias which may be seen in the syndrome However all of them can be produced when the same area in the A V node which allows the production of W P W complexes is made to function as the pacemaker At slow rates of stimulation extrasystoles occur When the stimulatory rate is increased so that it exceeds the rate of discharge of the S A node tachycardia results At still faster rates flutter and fibrillation appear These results in conjunction with those of Observation 5 demonstrate that the entire syndrome can be produced by alteration of a part of the A V node

Observation 7 Changes in Motion of the Ventricles During W P W Aberration and Their Correlation with Electrocardiographic Events

A pecial study was instituted in order to correlate the cardiac motions with their corresponding electrocardiographic manifestations Efforts in the past directed toward these ends have not provided much information Careful studies by means of electrokymography [39] analyses of arterial and venous pressure curves studies of heart sounds [3, 7, 15, 37, 40, 5-5] and investigations of intracardiac pressures [39, 56] have failed to demonstrate consistent correlation between the motions of the heart and the abnormal electrocardiogram in WPW aberration

The present investigation of this subject consisted of an analysis of cinematographs of the movements of the heart and simultaneous direct writing electrocardiograms filmed together This method enables the observer to ascertain the electrocardiographic significance of the actual movements of the heart The technique of this method has already been described (pages 9–12)

In this phase of the study WPW aberration was produced in 10

instances by non interrupted direct current applied to the epicardial or endocardial surface of the ventricles as described in Observation 4 In two experiments the aberration was produced by stimulating the A V node as in Observation 5

On several occasions alternating WPW complexes were produced It was found that for purposes of examining the cardiac motions during a WPW systole this type of aberration was the most useful since the alternate normal beats provided a striking contrast thus making comparison simpler

A study of the films reveals that WPW beats differ from normal beats in several important respects It was not possible to observe all the features of WPW beats in every heart The following is therefore a composite description obtained from a study of several hearts under different conditions

In both the normal and WPW beats the movements of the ventricular inflow tract are seen to be identical This is because the auricular contraction is the same in both The e movements are most clearly visible in the right ventricle since its wall is thin in comparison to that of the left ventricle and also because the right auricular systole is more vigorous than the left The ventricular inflow is seen as a distinct wave progressing from the right auricle to the ventricle starting at the A V groove and spreading caudally to the septum and apex In the normal beat when this motion has been completed there occurs a distinct pause Following this the ventricle contracts with a rapid smooth peristaltic motion starting at the apex and sweeps the blood to the pulmonary conus and into the pulmonary artery

These normal motions are in strong contrast to those of a WPW beat In the latter the pause that normally follows the completion of the inflow is absent Instead there is noted in the region surrounding the stimulating electrode a weak localized contraction of that part of the ventricle This weak contraction does not open the semilunar valve and expel blood from the ventricle It is best seen by timing it with the motion of the inflow tract

Shortly after the onset of the localized contraction of the stimulated area the rest of the ventricles are seen to begin their contraction As this contraction progresses the right ventricular motion appears sluggish and indecisive in comparison to the rapid motion of the normal ventricular contraction However although the sluggish con

traction of the ventricle in W P W beats appears in the films to be very distinct it may be more apparent than real. It is possible that this appearance may be caused by a distortion of the main ventricular contraction wave by the presence of the area of localized contraction which tends to obstruct its passage and cause it to detour. Moreover the main contraction may be a little weaker than normal since a part of that ventricle has already contracted.

Toward the end of systole the localized area which had contracted prematurely enters its diastolic phase. Since the duration of its systole is approximately the same as that of the main contraction this early localized diastole occurs while the major portion of the ventricles is still contracting. As a result of the high intraventricular pressure present during this phase and because the localized area is in diastole its wall undergoes a marked outward protrusion. The surface of this bulging area becomes distinctly whitened. From the boundaries and extent of the area of protrusion it becomes clear how large an area had been stimulated and had contracted prematurely. This diastolic ballooning area is more plainly visible than the actual systolic contraction which is weak and less distinct. In these experiments its size usually approximated $\frac{1}{8}$ of the total ventricular area.

The duration of systole of the localized area of premature contraction and that of the normally contracting portions of the ventricles are apparently equal. As represented in the diagram (Figure 25) the contraction of the localized area begins before that of the normal area and its relaxation occurs before the relaxation of the normal area.

It is thus evident that the total duration of ventricular systole is longer in a W P W beat than it is in a normal beat.

From the above observation it can be seen that a ventricular systole of the W P W type may consist of four separate phases: *First*, premature contraction of a limited area of one ventricle; *second*, contraction of the remainder of the ventricle (through the normal mechanism); *third*, diastolic relaxation and protrusion of the prematurely contracted area while the remaining part of the ventricle are still contracting; *fourth*, relaxation of the rest of the ventricle.

All of these features cannot be demonstrated in every W P W beat of every heart studied. In certain instances, to be discussed later, some of these characteristics appear to be lacking.

Having become familiar with the most significant kinetic phenom

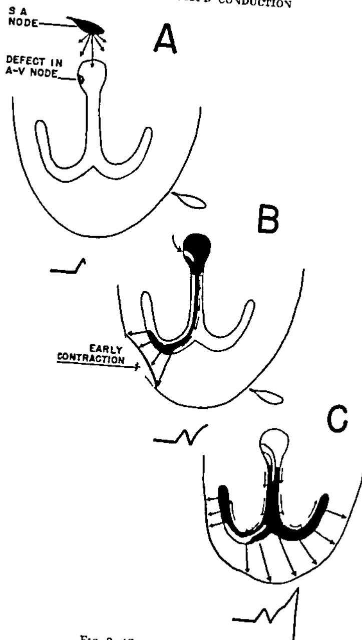


FIG 25 (*See legen l on page 47*)

ena occurring during WPW aberration it is now possible to correlate these motions with the corresponding electrocardiographic events On the projected cinematographs the heart and the electrocardiogram are seen side by side as the motions of the former occur the tracing of the latter is observed as it is being written

The first important information obtained from this combined study is that the early localized ventricular contraction involving the area which has been stimulated corresponds with the appearance of the first slurred portion of the R wave The shortening of the P R interval and the characteristically deformed upstroke of the R wave which is typical of WPW complexes is shown in Figure 26A When the rest of the ventricular contraction occurs the major portion of the R wave arises and is then superimposed on the early R In figure 26B is seen the completion of the R wave late in systole and the protrusion of the prematurely contracted area This sequence of events results in the wide and aberrant ventricular complexes usually seen in the WPW syndrome Diastole of the entire heart is shown in Figure 26C Figure 27B demonstrates the ballooning effect in another heart in Figure 27A this is absent

Additional information concerning the R wave may be obtained by a correlation of the extent of the ventricular area which contracts early and the width of the early R wave which occurs with it As already noted the area which contracts before the rest of the ventricles presents a marked bulge and whitening during its relaxation This makes its extent obvious and it was observed that the larger

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FIG 25 —Diagrammatic representation of hypothetical mechanism of accelerated conduction

(A) The impulse originating in the S A node is spreading over the auricle while the P wave is being written

(B) The defect or disturbance in a part of the A V node has permitted part of the impulse to pass through this portion of the node prematurely and to activate prematurely a small area of one ventricle This activation and the resulting premature localized contraction are associated with the inscription of the early slurred portion of the R wave

(C) After the normal delay at the A V node the remainder of the impulse has passed down the bundle of His to the rest of the ventricles and has activated them normally This activation and the resulting normal contraction are associated with the inscription of the normal portion of the R wave Note that the area of premature contraction is now bulging since it is in its diastolic phase while the rest of the heart is in systole





B



C

this area of early contraction the wider the early R wave associated with it and the shorter the P R interval When large areas were involved and the early R wave was wide the entire ventricular complex was therefore wide and conversely the smaller the area of early contraction the longer the P R interval and the narrower the early R hence the more normal the whole ventricular complex The correlation of these findings with the variations in configuration of the QRS complexes observed clinically in WPW aberration will be discussed later It may be said however that the degree of aberration of the complex depends upon the location of the prematurely contracting area and the degree of prematurity of its contraction

It has been demonstrated that in the WPW complex there is a localized area in one ventricle which contracts prematurely and that this early contraction accounts for the short P R interval the deformation of the R wave near its inception and the widening of the QRS complex It thus becomes evident that this area of premature contraction provides the basis for the entire WPW aberration It is also clear that the WPW complex is a fusion beat composed of the premature contraction of a localized portion of one ventricle together with the normal beat

In the two experiments in which photographs were made of the WPW aberration produced by stimulating the A V node rather than the ventricle proper the QRS complexes were normal but the P R interval was shortened In these instances the films did not reveal a premature localized contraction and it would appear that there occurred a normal but premature contraction of all of both ventricles

FIG 2b (*See facing page*)

(A) Frame from high speed cinematograph of heart and simultaneous electrocardiogram of a dog during a WPW beat showing the premature localized contraction of the ventricle occurring at the same time as the inscription of the premature first portion of the R wave Note the short P R interval The part of the ventricle which is contracting prematurely is outlined

(B) Later frame of same beat showing the completion of the contraction of the rest of the ventricles occurring at the same time as the completion of inscription of the remainder of the R wave

(C) Still later frame of same beat showing the heart in full diastole The isoelectric period of the electrocardiogram has just ended and the P wave of the next beat is just beginning

Camera speed 5000 frames per second Electrocardiograph paper speed 125 mm per second

A



B



Fig. 27.—(A) Frame from high speed cinematograph of heart of a dog and simultaneous electrocardiogram. The stimulating electrode is in place (upper left).

(B) The stimulating current has now been turned on and a WPW beat is occurring. The heart is in the same phase of systole as in (A). The protrusion of the area of premature contraction can be seen in the upper left portion of the heart about the electrode (the right ventricle above the septum). The electrocardiogram is nearing the completion of the inscription of the WPW complex.

Camera speed 200 frames per second. Electrocardiograph paper speed [illegible] mm per second.

This would account for the normal QPS complexes Unfortunately no films were made of tho e WPW beats resulting from nodal stimu lation in which the QRS was widened

In the foregoing experiments mo t of the clinical varieties of WPW aberration were photographed These include isolated WPW beats continuous WPW aberration WPW beats alternating with normal beats the concertina effect WPW complexes showing QRS com ponents of various configurations and WPW complexes originating from the epicardial and endocardial surfaces of either ventricle or from the septal region If the location of the premature contraction and its degree of prematurity are known the general characteristics of the aberrant complex can be predicted

By means of a new technique utilizing high speed cinematography the details of ventricular movements in the W PW aberration have been studied and correlated with their corresponding electrocardiographic events The most significant observation was that the usual forms of W PW aberration in these experiments are due to an early ueal local i ed contraction of a portion of one ventricle followed by the normal systole of the rest of the ventricles It was also found that the premature slurred portion of the R wave is associated with the premature locali ed contraction and that the W PW complex as a whole is the result of fusion of this contraction with the contraction of the rest of the ventricles The differences which occur in various forms of W F W complexes may be explained by two factors the location of the prematurely contracting area and the degree of prematurity of its contraction

Observation 8 The Role of Normal A V Conduction in the Pathogenesis of W PW Complexes

The stimulus producing the aberrant complexes in all the above experiments (Observations 1–7) was purposely applied at points remote from the auriculoventricular groove In this way any aberrant anatomical pathway as yet described could not have been stimulated The production of WPW complexes in these experiments therefore appeared to be independent of such anomalous connections and re ulted rather from the pas age of impul es over the normal conduc tion system in some abnormal manner

This hypothesis is susceptible to direct experimental testing in accordance with the following reasoning There are two possible modes

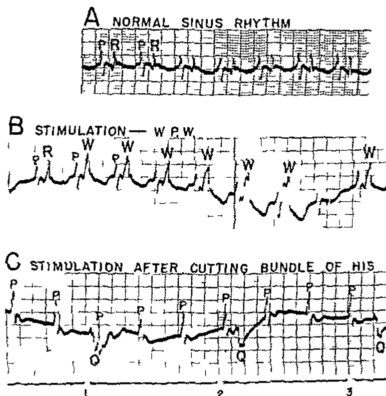


Fig 28 —(A) Normal sinus rhythm in a dog Direct auricular lead
(B) WPW aberration produced in the same animal by uninterrupted electrical stimulation of the endocardial surface of the right ventricle Direct auricular lead
(C) Complete heart block after section of the bundle of His in the same animal failure to produce WPW aberration by the same method which was successful in (B) The ventricular complexes are due to idioventricular rhythm and follow P waves only by chance Direct auricular lead

of transmission of the auricular impulse to the ventricles The first is by way of anomalous anatomical A V connections such as the bundle of Kent The other possibility is that the impulse passes in an abnor

mal manner over the normal conduction system If the first mechanism is correct then interruption of the anomalous pathway should prevent the production of WPW complexes However it is impossible to interrupt all the possible anomalous connections On the other hand

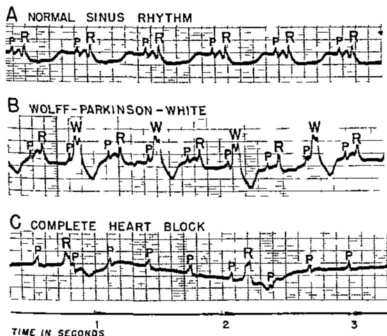


FIG 29—(A) Normal sinus rhythm in a dog Direct auricular lead
(B) WPW complexes alternating with normal complexes produced in the same animal by uninterrupted electrical stimulation of the endocardial surface of the right ventricle at the apex Direct auricular lead
(C) Complete heart block after section of the bundle of His in the same animal failure to produce WPW aberration by the same method which was successful in (B) The ventricular complexes are due to idioventricular rhythm and follow P waves only by chance Direct auricular lead

interruption of the normal conduction system is perfectly feasible and should not interfere with the production of WPW aberration Therefore the hypothesis was tested by attempting to produce WPW aberration after severing the bundle of His

In each of seven dogs runs of WPW complexes were produced by direct electrical current stimulation of the endocardial surface of the right ventricle as in Observation 4 A small ball tipped cautery was then inserted through a second opening in the right auricle and passed through the tricuspid valve into the right ventricle The bundle of His was then severed by the cautery as shown by the appearance of complete heart block

Attempts were then made to produce WPW complexes in exactly the same manner as before but even when the stimulating current was quadrupled in intensity *in no instance did these complexes occur* (Figures 28 and 29)

The tracings obtained after the production of complete heart block showed idioventricular beats but these did not follow P waves except by chance (Figures 28 and 29) This experiment demonstrates the impossibility of producing WPW complexes without an intact bundle of His If anomalous bundles transmitted the impulse from the auricles to the ventricles and were responsible for the aberrant complexes severing the bundle of His should not have interfered with the production of these complexes In fact the elimination of the normal conduction pathway would be expected usually to aggravate the aberration since the complex would then have to be produced entirely by way of ectopic channels

It will be recalled that in Observation 5 WPW complexes were produced by stimulating the A V node It is clear that in those experiments also the impulse must have passed down the bundle of His rather than through aberrant anatomical pathways It is obvious therefore that if the bundle of His had been cut as in the present experiment and the A V node then stimulated WPW complexes could not have been produced

WPW complexes were produced in these experiments by stimulation of the ventricle as in Observation 4 The bundle of His was then severed After this procedure it was impossible to produce WPW complexes with the same method which had been successful previously in the same dog This observation provides direct evidence that the impulse in the WPW complex traverses the normal conduction pathways and does not depend upon anomalous A V connections This is true whether the aberration is produced by stimulation of the ventricle or of the A V node

CHAPTER IV

Accelerated Conduction

Nodal and Ventricular Types of WPW Aberration

WPW ABERRATION may be of nodal or of ventricular origin It will be recalled that in Observation 5 WPW aberration was produced by continuous electrical stimulation of the *A V node* This may therefore be called the nodal type of WPW aberration

In Observations 1 2 and 4 however WPW aberration was produced by mechanical chemical and electrical stimulation of the *ventricles* Aberration thus produced from a ventricular focus may be termed the ventricular type

Both the nodal and the ventricular types are of clinical as well as physiological importance

The electrocardiographic characteristics of these two types of aberration appear to be identical and the P waves in both are normal However they differ in that the ventricular type may be accompanied by ventricular extrasystoles and ventricular tachycardia while the nodal type is not When the area in the A V node responsible for the nodal type becomes the pacemaker as in Observation 6 supraventricular arrhythmias especially tachycardia occur

The nodal type thus duplicates the clinical WPW syndrome since (1) the usual form of WPW aberration results when the node is altered (2) all the supraventricular arrhythmias associated with the syndrome occur when the same area in the node becomes the pacemaker and (3) ventricular extrasystoles and ventricular tachycardia do not occur

The ventricular type of WPW aberration also has its clinical applications It has already been seen that this form of aberration may occur in human subjects during catheterization of the heart (Observation 1) There are several other conditions in which WPW aberration appears to arise from a ventricular focus These will be discussed later

It has been shown that the aberration occurring in the clinical WPW syndrome may assume a variety of forms. Each of these has been reproduced in the experimental animal. The various kinds of WPW aberration seen clinically and produced in this investigation include continuous WPW aberration, isolated WPW beats, WPW complexes alternating with normal complexes, runs of WPW complexes exhibiting the "concertina effect," WPW complexes having QRS components of various configurations, WPW complexes showing only very slight aberration, and WPW complexes with normal QRS components. During the experimental production of these different types of WPW aberration it was noted that in general the form of the aberrant QRS complex depended upon the location of the area stimulated. Thus it would appear that a complete clinical correlation was provided experimentally.

In Observation 8 it was demonstrated by a direct experimental method that WPW aberration cannot be produced when the bundle of His is severed. The impulse responsible for this aberration must therefore pass from the auricles to the ventricles over the normal conduction system and not by way of anomalous anatomical pathways. As pointed out above (page 54) this holds true for both the nodal and ventricular types of WPW aberration.

Kinetics of WPW Aberration

By means of high speed cinematography (Observation 7) motions of the heart in WPW beats were studied in great detail and compared to those of normal beats. Thus the kinetic disturbances characteristic of WPW beats were actually observed directly. The essential abnormality most commonly seen was a premature localized contraction of part of one ventricle. This contraction was weak and did not cause opening of the semilunar valves. The early contraction was quickly followed by the contraction of the rest of the ventricles at the normal time. It was seen that the area which had contracted prematurely relaxed while the normal contraction was still in progress. Hence the usual WPW beat appears to consist of four phases—(1) premature contraction of part of one ventricle, (2) contraction of the rest of the ventricles at the normal time, (3) diastolic relaxation of the area of first contraction, and (4) diastolic relaxation of the rest of the ventricle.

Correlation of Electrocardiographic and Kinetic Changes in WPW Aberration

With the aid of the combined electrocardiographic cinematographic technique the minute details of the genesis of the electrocardiographic features of WPW beats were studied and correlated with the simultaneous movements of the heart In this way it was seen that the premature localized contraction in the ventricle is associated with the premature appearance of the R wave (short P R interval) and the slurring of the initial part of the R wave The contraction of the rest of the ventricular mass which then follows corresponds with the rest of the R wave Hence the R wave is both early and wide It was also observed that in general the larger the area of premature contraction the wider the R wave

Thus from direct simultaneous visualization of both the mechanical and electrocardiographic events it was apparent that WPW beats are actually fusion beats They have the unique characteristic of being composed of (1) an early localized contraction of one ventricle and (2) the normal contraction of the rest of the ventricles

Observation of the films and electrocardiograms revealed many other features having clinical application All the various forms of WPW aberration known to occur clinically were actually watched as they were being produced Isolated WPW beats continuous WPW aberration WPW beats alternating with normal beats and all the other forms previously mentioned were seen during the process of their production

It was seen also that the localized area of the ventricle contracted with various degrees of prematurity Furthermore the location of this area was also variable depending upon the point of application of the stimulus Thus we have two factors the degree of prematurity of the localized contraction and the site of this contraction which together may serve to explain the numerous variations in the configuration of the QRS complexes observed in clinical instances of WPW aberration For example if the localized area of contraction is small and situated far from the septum and if the degree of prematurity of this contraction is not marked the rest of the ventricles are activated by the normal impulse This combination of circumstances was present in the experiments and was observed in the films Since the second contraction occurs at the normal time the P R interval will be the same as

the P J interval of normal complexes of the same animal Experimentally this is the most common type of WPW beat Likewise in the clinical WPW syndrome the P J interval of WPW beats are in most instances equal to those of normal beats occurring in the same patient Therefore it may be reasoned that in the usual clinical case the area of premature contraction is situated at a distance from the septum and does not contract very prematurely

In rare instances such as those observed by Kossmann and Goldberg[1 b] and Wolff and White[1 a] the P J interval of WPW complexes are shorter than the P J intervals of normal complexes occurring in the same patient The location of the area of premature contraction and its degree of prematurity may account for this finding in either of two ways First if the prematurely contracting area happens to be located on or near the septum the entire mass of both ventricles will be depolarized prematurely before the normal impulse has arrived In this event the normal impulse will be blocked by refractory tissue and will not cause a contraction A septal location of the premature contraction which causes premature contraction of the whole ventricular mass may also account for those WPW complexes having QRS components of normal width Clinical examples of this form of WPW aberration have been described[57] Evidence supporting this explanation is found in the demonstration that ectopic beats and ventricular tachycardia arising in the septal region may have QRS complexes of normal width[45] A modification of this mechanism may also account for the occurrence of narrow QRS complexes in WPW aberration for a premature but otherwise normal contraction of both ventricles might result from an alteration of the whole A V node This phenomenon appears to have taken place in the two instances in Observation 7 in which cinematographs were taken while the A V node was being stimulated In these films the entire ventricular contraction was apparently normal although premature and the corresponding QRS complexes were not widened It may be that a similar mechanism is responsible for the group of cases described by Lown Ganong and Levine[9] in which the P R intervals were short, the QRS complexes were of normal width and paroxysms of supraventricular tachycardia were common

The second condition which can account for short P J intervals in WPW aberration occurs when the localized area of premature contraction is activated very prematurely In this case even though this

area be situated far from the septum the impulse might spread to the rest of the heart including the opposite ventricle before it can be activated by the normal impulse This too would result in a premature contraction of the entire ventricular mass thus producing a short P J interval The QRS complex in such a beat however will be very wide and resemble an idioventricular extrasystole arising at the same site except that it closely follows a P wave

One of the forms of WPW aberration produced in Observation 4 manifested only minor changes in the QRS complexes These were best recorded by direct ventricular leads the limb leads either did not pick them up at all or revealed only a small change in the height of the R waves and a very slight shortening of the P R intervals Complexes of this kind showing practically imperceptible abnormalities might result from a minute area of premature contraction which is activated only slightly earlier than normally Clinical examples of this form of minor WPW aberration are not rare but may be overlooked because of the minor degree of ventricular aberration Patients with this embryonic form of the syndrome may develop paroxysms of auricular tachycardia in the same manner as those with more obvious forms of WPW aberration We have seen cases of so-called idiopathic or familial paroxysmal auricular tachycardia in young adults whose tracings on careful examination during sinus rhythm disclosed slight slurring of the upstroke and the R waves These are probably instances of this form of the WPW syndrome In his monograph Ohnell[3] emphasizes the familial tendency to paroxysmal auricular tachycardia in association with the WPW syndrome he states that out of five members in one family who had this arrhythmia four had WPW aberration during sinus rhythm while the other had a normal electrocardiogram In another family five siblings had paroxysmal auricular tachycardia and two of these had WPW aberration the remaining three did not It seems probable that the members of these families who were subject to bouts of auricular tachycardia but apparently showed no WPW aberration during sinus rhythm may actually have been examples of this embryonic form of the syndrome The importance of recognizing the existence of this embryonic form of the WPW syndrome lies in the possibility that it may explain many cases now considered idiopathic or familial tachycardia

Because of the premature activation of one ventricle in WPW

beats the question of asynchrony of ventricular contraction in the e beats has been examined by several investigators [7, 3, 55, 63] More recently Dack and his associates [39] in a carefully executed electrokymographic study were unable to detect any asynchronism in the ejection phases of right and left ventricular systole in four patients with the WPW syndrome This finding may be explained by the cinematographic observation that the premature contraction is small and weak Such a contraction did not cause opening of the semilunar valve and did not expel blood into the pulmonary artery or aorta Rather than opening the semilunar valve the slight pressure exerted by the premature contraction was probably manifested by an imperceptible bulge in the rest of the ventricle Since as pointed out above in the usual patient with the WPW syndrome the premature contraction is also small and weak no outflow will occur until the contraction of the rest of the ventricles at the normal time This explains the observation of Dack et al that the ejection of blood from both ventricles may take place simultaneously in spite of the premature excitation of part of one ventricle which occurs in the usual case with WPW aberration As pointed out above under other circumstances both ventricles may also contract simultaneously in a WPW beat

It is apparent that the occurrence of narrow QRS complexes in WPW beats is confusing and requires further clarification This phenomenon is observed in a number of clinical conditions and may be produced experimentally in three different ways The first and most important of these is by direct stimulation of the A V node The *resulting WPW complexes may have QRS components* of normal width and configuration and the P R intervals are short This form of WPW complex corresponds to the type noted by Lown Ganong and Levine[9] in patients subject to paroxysms of supraventricular tachycardia whose tracings during sinus rhythm show normal QRS complexes and short P R intervals Narrow QRS complexes may also be produced by stimulation of the epicardial surface of the ventricles over the septum These QRS complexes however are not normal in configuration since the ventricles although activated simultaneously are excited in an abnormal sequence The third manner in which narrow QRS complexes can be produced in WPW aberration is by stimulation of the ventricle proper far from the septum with a weak

electrical current This sometimes gives rise to WPW complexes of normal width but having very slight alteration in configuration The P R intervals in these complexes show little or no shortening Clinically this form of WPW aberration may differ so little from the normal that the diagnosis may be impossible

The Excitation Pathway in WPW Aberration The Normal Conduction System versus Anomalous Anatomical Pathways

In Observation 8 it was shown by the direct method of interrupting the bundle of His that WPW aberration could not be produced without an intact normal conduction system and that therefore the impulse in WPW complexes did not reach the ventricles by way of anomalous anatomical A V connections

Even before this experiment was undertaken the results of Observations 1 2 and 4 had cast serious doubt on the possibility that anomalous pathways could be involved in the transmission of impulses in WPW complexes In these experiments the WPW aberration was produced by various forms of stimulation of the ventricles in regions far removed from the A V groove Under these circumstances if the presence of anomalous A V pathways is assumed then the deliberate avoidance of stimulation in the region which they must traverse would have precluded the possibility that they could have been stimulated directly When it is considered that WPW complexes were produced in practically every dog used in these experiments and that WPW complexes also develop in many human patients without the WPW syndrome when they undergo cardiac catheterization there is still further reason to doubt the existence of functioning anomalous anatomical pathways If such pathways were responsible for the aberration it would be necessary to assume that (1) they are present in almost all dogs and men (2) they are ordinarily dormant and non functioning (3) they may suddenly become active as a result of various procedures taking place far from their presumed location and (4) when the procedure is finished they resume their dormant state It is highly improbable that such a group of conditions can exist

The demonstration that WPW aberration in these experiments

takes place through normal channels indicates that the WPW phenomenon may properly be considered a physiologic rather than an anatomic disturbance

The Nature of the Human WPW Syndrome and a Consideration of the Arrhythmias Associated with It

The exact localization of the disturbance responsible for human WPW aberration is a matter of considerable interest In Observation 8 it was seen that WPW aberration can be produced by stimulation of the A V node With continuous stimulation of subthreshold intensity where the auricles were driving the ventricles WPW complexes of various types were produced all had short P R intervals and normal P waves Therefore it may be said that an alteration in the A V node can give rise to the usual clinical form of WPW aberration When this same altered area in the node becomes the pacemaker by stimulating it with interrupted current all the arrhythmias which may occur in the clinical syndrome can be produced successively by progressively increasing the rate of stimulation These arrhythmia are nodal extrasystoles nodal tachycardia flutter and fibrillation Electrocardiograms demonstrating the nodal origin of each of these arrhythmias (with the exception of fibrillation in which the origin cannot be determined from the tracings) occurring in patients with the WPW syndrome have been published by several authors[3, 38] Examples of flutter and fibrillation in both patients and dog are shown in Figures 30 and 31 It is clear that the human and animal tracings are identical in all important respects Neither the experimentally produced arrhythmias in animals nor those occurring spontaneously in man can be explained by the theory of anomalous anatomical bundles This theory attempts to explain the auricular tachycardia of the WPW syndrome on the hypothesis that retrograde ventriculo auricular conduction with a 1 1 ratio is responsible for the arrhythmia But as has been pointed out the production of flutter and fibrillation in this manner would require ventricular rates as high as 300 and 400 respectively The adult human ventricles however cannot respond so rapidly except under the most unusual circumstances

In the cinematographic observations it was seen that the premature contraction in WPW complexes usually involved only part of the

ventricle Therefore it can be reasoned that the disturbance which permits premature passage of the auricular impulse to the ventricle must involve only part of the node This hypothesis requires that four conditions be fulfilled (1) There must normally be a delay of the auric-

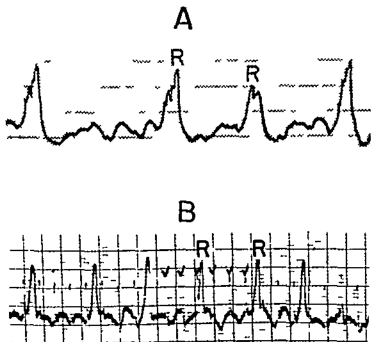


FIG 30 —(A) Paroxysmal auricular fibrillation occurring spontaneously in a patient with the WPW syndrome Lead 3

(B) Paroxysmal auricular fibrillation produced experimentally in a dog by interrupted electrical stimulation of the same area in the A V node which previously resulted in WPW aberration when stimulated by an uninterrupted electrical current as in Fig [illegible] (C) Lead 3

ular impulse at the A V node (2) in WPW aberration the normal delay takes place except at that part of the node which has been altered This altered portion must allow part of the impulse to pass through without the normal delay (3) the abnormal impulse must pass down the bundle of His and (4) the A V node and bundle must

be constituted in such a way that specific cells or areas of the node supply specific areas of the ventricular myocardium

With reference to the first of these requirements there has been considerable controversy concerning the location of the delay which





FIG 31 —(A) Paroxysmal auricular flutter occurring spontaneously in a patient with the WPW syndrome Lead 3 The inverted P waves indicate that the flutter arises low in the auricle

(B) Paroxysmal auricular flutter produced experimentally in a dog by interrupted electrical stimulation of the same area in the A V node which previously resulted in WPW aberration when stimulated by an uninterrupted electrical current Lead 3 Note the similarity of this experimentally produced flutter to the spontaneously occurring human flutter in (A)

normally occurs in the passage of the auricular impulse to the ventricular myocardium [13, 4–45, 61] There is no doubt that this delay occurs at some point between the site of entrance of the impulse into the A V node and the ventricular myocardium This must be true

since the time required for the excitation wave to traverse the auricle accounts for only a small fraction of the total time which elapses between the moment of origin of the impulse at the S A node and the moment of onset of ventricular depolarization. The difficulty in determining the site of the delay more closely has arisen because there is no way of detecting the impulse as it passes down the conduction system. Consequently, two theories attempting to localize the site of delay have been propounded. The first of these, originating with Sir Thomas Lewis, postulates that the impulse is slowed in passing through the A V node and then progresses rapidly down the bundle of His, the bundle branches and the Purkinje system to the ventricular musculature where it causes immediate depolarization. The other theory, known as the "latency theory," maintains that the delay does not result from retardation of the impulse at the node but at the terminal endings of the Purkinje system.[61] After this delay has been overcome, ventricular depolarization takes place.

A recent investigation in this laboratory[16] designed to determine the site of the normal delay in auriculo ventricular conduction seems to have provided an answer to this question. This was accomplished by stimulating with interrupted electrical current, first the bundle of His and then the A V node. If the impulse so produced were delayed at the terminal endings of the Purkinje system, there should be no appreciable difference in the time interval between the moment of stimulation and the onset of ventricular depolarization, whether the stimulus were applied to the bundle or to the node. Measurements of the interval between the instant of stimulation and the onset of the P wave of the electrocardiograms resulting from stimulating these two structures, however, showed that these intervals were significantly longer when the impulse had to pass through the node than when it originated in the bundle. This direct experiment demonstrates, therefore, that the delay in normal A V conduction occurs at the A V node and not at the periphery of the conduction system. Hence the A V node has the *important* function of delaying auricular impulses. If it were not for this function the auricles and ventricles would contract practically at the same time and the auricles would become functionally useless.

The second requirement of the theory demands that this normal retardation of the impulse is partly overcome in W P W beats. This is

evident from the direct visualization of the prematurity of the R wave It is also clear from the cinematographic observation that the pause which normally follows the completion of auricular contraction is in WPW beats partially abolished by the early localized contraction of one ventricle which is responsible for the early R wave The remainder of the ventricles then contracts normally after the normal delay *

The third requirement of the theory that the impulse must pass down the normal conduction system in WPW aberration has been proven in direct experiment in Observation 8 where it was found impossible to produce WPW complexes after cutting the bundle of His using the same method of stimulation that had produced such complexes with an intact conduction system

Finally if a portion of the A V node is altered in such a way that it allows premature transmission of impulses to a part of one ventricle it is necessary to show that the node and bundle are constituted so that a given region of the node sends impulses to the same specific region of the ventricle That this is actually so is strongly suggested by the finding in Observation 5 that stimulation of a fixed area of the A V node always gives rise to WPW aberration of the same configuration Furthermore experiments now being conducted in this laboratory indicate that specific areas of the ventricles can be blocked by interrupting the branch of the bundle supplying it The results of this work suggest that the bundle of His is composed of long tracts of conducting fibers arranged much like those of the spinal cord Hence it appears that a given area in the A V node through a fixed pathway will always supply the same localized area of the ventricle and no other Although direct experimental correlation of specific areas in the node with corresponding areas in the ventricle is difficult because of the small size of the nodal areas under investigation compared for example to analogous areas in the brain further study of this subject is obviously necessary

* It may be theorized that this abolition of normal delay can take place in either of two ways The first possibility is that there exists some kind of alteration of a portion of the node which permits the impulse to traverse it more rapidly than normal The other possibility is that there is no increase in the velocity of the impulse but that it enters the node lower than does the normal impulse Thus it would have less distance to travel within the node and would enter the ventricle prematurely

It has been shown in the preceding paragraphs that (1) the auricular impulse normally undergoes a delay at the A V node (2) in WPW complexes this delay is partially abolished (3) the excitation impulse in WPW complexes passes from auricles to ventricles via normal channels and (4) the A V node and bundle of His are arranged functionally at least so that specific cells or areas in the node appear to send impulses to specific areas of the ventricle The theory that the premature contraction of part of one ventricle in WPW aberration is due to an alteration of part of the node allowing premature transmission of the impulse to this part of the ventricle therefore becomes tenable and attractive

Semi quantitative Estimation of Loss of Delay in WPW Complexes

In a previous investigation the passage of the impulse from the S A node to the A V node was timed by means of two esophageal leads placed nearly opposite these structures The results of this study indicate that the impulse arrives at the lower electrode approximately 0 05 second after its onset Actually the distance between the two nodes is such that the time needed for the impulse to traverse the auricles would be closer to 0 06 or 0 07 second Therefore if no delay intervened between the moment of arrival of the impulse at the A V node and the moment of ventricular depolarization the P R interval would be 0 06 or 0 07 second This is the minimum P R interval possible in WPW complexes if as stated by the theory of accelerated conduction the impulse utilizes the normal channels A P R interval of less than 0 06 second would suggest a shorter A V pathway such as might be provided by an anomalous connection The reported P R intervals of large groups of cases in the literature was therefore examined in order to determine the shortest P R interval recorded in WPW complexes It was found among a series of 41 cases studied by Wolff and White[12] that the shortest P R interval measured 0 07 second We have often seen P R intervals of 0 07 second in WPW complexes in dogs but have not observed any which have been less than this either in animals or in man This finding is an interesting bit of evidence which tends in an indirect manner to corroborate the accelerated conduction theory This minimum P R interval is observed when all the delay normally present at the A V node has been

abolished Hence it may be postulated that in cases with P R intervals of 0 07 second the WPW disorder is 100 per cent complete and no delay occurs at the node

Knowing the time required for the impulse to travel from the S A node to the A V node to be approximately 0 07 second it is possible to estimate the severity of the WPW condition in any given case First the P R interval of a normal complex of the same patient is measured This may be for example 0 19 second Of this 0 19 second, 0 07 second is occupied by the passage of the impulse from the S A node to the A V node the remainder 0 12 second is the duration of the delay at the A V node The same procedure is now followed for a WPW complex A P R interval of 0 11 second for this complex may be found Subtracting 0 07 second from this figure a delay of 0 04 second at the A V node is evident This delay may be expressed as a fraction of the delay in the normal complex and in this instance is $\frac{4}{12}$ or $\frac{1}{3}$ of the normal The WPW disorder may therefore be said to be approximately $\frac{2}{3}$ complete In the same manner the severity of the abnormality may be roughly estimated for any WPW complex if the P R interval of a normal complex of the same patient is known

The Theory of Accelerated Conduction

It has been shown in the preceding discussion that part of the auricular impulse in WPW complexes undergoes less delay at part of the A V node than does the impulse in normal complexes Stated conversely this means that part of the impulse passes through part of the node in less time than normal The possible nature of the abnormal process at the A V node permitting this phenomenon will be more fully discussed later for the moment the important point is that part of the excitation wave in WPW complexes arrives at the ventricular end of the node sooner than the rest of the impulse In whatever manner this process comes about it may be looked upon as *accelerated nodal conduction* It is suggested that this term be employed where applicable since it indicates more exactly the nature of the disturbed physiological function than other terms now in use

The WPW syndrome a congenital anomaly and consisting clinically of various forms of ventricular aberration associated with the paroxysmal supraventricular arrhythmias is the best known example of accelerated conduction As this condition is a clinical entity it may

be termed The Accelerated Conduction Syndrome Each aberrant beat however may be called an accelerated conduction beat As will be shown there are several other conditions not constituting a part of this syndrome which are nevertheless brought about by the mechanism of accelerated nodal conduction The aberrant complexes occurring in these conditions may also be designated as accelerated conduction beats This term which describes the physiological disturbance would appear preferable to such expressions as WPW beats pre excitation beats and other miscellaneous terms presently in use

CHAPTER V

Clinical Significance of Nodal Type of Accelerated Conduction

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IT WILL BE RECALLED that experimentally there were produced two general types of accelerated conduction beats the nodal and the ventricular The e two types of accelerated conduction may also be distinguished clinically The nodal type is characterized by a primary disturbance in the A V node which is responsible for the disorder In the ventricular type however the disturbance originates in the ventricle How the phenomenon of accelerated conduction is brought about in this type is not known but it may be speculated that the ventricular focus might by means of antidromic impul es, give ri e to a secondary disturbance in the A V node which permits accelerated conduction

Con idering first the nodal type of clinical accelerated conduction evidence has been presented that the classic WPW syndrome is an example of this group This is most likely due to a congenital anomaly and has been thoroughly considered elsewhere

Among the other conditions characterized by accelerated conduction of nodal origin is the ventricular aberration sometimes observed in the course of certain auricular arrhythmias As pointed out in previous investigations [1] this type of ventricular aberration may occur in any of the auricular arrhythmias but is seen most frequently in as o ciation with auricular extrasystoles flutter and fibrillation An example of uch aberration occurring as it does so frequently in auricular flutter is seen in Figure 32 In several re pects it is similar to the aberration een in the accelerated conduction syndrome (1) The QRS complex is distorted or widened (2) the shape of the QRS complex is directly related to the length of the P R or P R interval (3) many patterns of aberration may occur (4) the T waves are altered, and (5) when complete heart block is present no ventricular

aberration of this type exists The validity of this last observation is supported by the clinical finding that in auricular tachycardia and flutter with complete heart block ventricular aberration of this type is ab ent [1] Ventricular aberration occurs frequently in auricular fibril

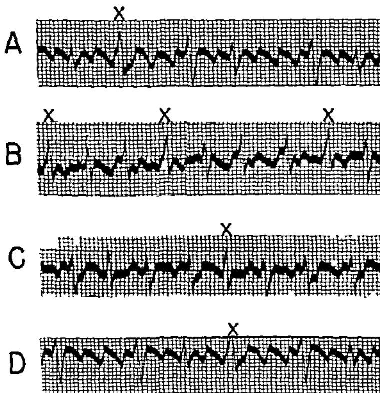


FIG 32 —Examples of ventricular aberrati n occurring in 4 different patients during auricular flutter Th aberrant ventricular complexes indicated by an X resemble the ventricular complexes of W P W beats Lead 3

lation but in our experience it is not seen in ca es of fibrillation with complete heart block Thus it appears that the ventricular aberration associated with auricular arrhythmias is mediated through the normal conduction system Because of its close resemblance to the aberration pre ent in the accelerated conduction syndrome it is suggested that

this type of aberration results from the same physiological disorder—accelerated nodal conduction In this instance the disturbance may well be produced by the abnormal bombardment of the A V node by auricular impulses causing the node to discharge abnormally It is possible also that accelerated conduction may be brought about by reflex changes affecting the A V node as suggested by the following cases

CASE 1 This patient was hospitalized because of a bronchogenic carcinoma involving the left lung After the usual studies a left pneumonectomy was performed A continuous electrocardiogram was made during the operation This revealed normal complexes until the surgeon exerted traction on the pulmonary artery Whenever this manoeuvre was carried out runs of accelerated conduction beats appeared when the traction was released normal complexes promptly reappeared as shown in Figure 33

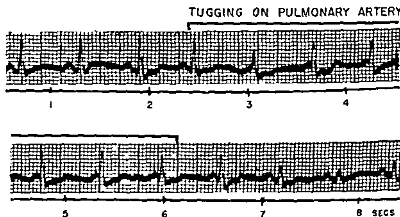


Fig 33—Accelerated conduction complexes produced by tugging on the pulmonary artery of a patient during an intrathoracic surgical procedure When the traction on the pulmonary artery was released normal conduction resumed Standard limb lead

CASE 2 This patient also underwent left pneumonectomy for bronchogenic carcinoma Continuous electrographic tracings were made during the operative procedure No abnormal complexes were observed until traction was applied to the left auricular appendix at which time occasional isolated accelerated conduction beats appeared (Figure 34)

While it would seem most likely that accelerated conduction in these cases resulted from reflex mechanisms affecting the A V node further investigation will be required in order to clarify the relation of reflex changes to the phenomenon of accelerated conduction

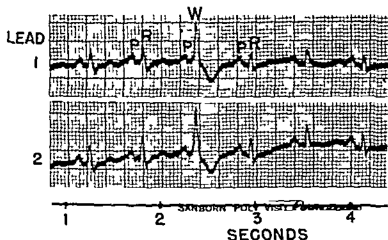


Fig 34 —Simultaneously recorded leads 1 and 2 showing an isolated accelerated conduction beat produced by tugging on the left auricular apper lix of a patient during an intrathoracic surgical procedur

Acquired Types of Accelerated Conduction Due to Disease of the A V Node

A very important example of accelerated conduction beats of nodal origin and one needing much study is the occurrence of this type of beats after myocardial infarction and other lesions involving the A V node During the past year we have observed seven cases probably of this nature Six of the e were instances of posterior wall infarction None of these patients developed ventricular extrasystoles or ventricular tachycardia

CASE 3 The patient was a 42 year old man who gave a typical history of myocardial infarction occurring on February 20 1951 The first electrocardiogram made on admission to the hospital revealed continuous accelerated conduction complexes (Figure 35A) Later the tracing showed runs of accelerated conduction beats interspersed with normally conducted

be its (Fi_gure 3oB) Subsequent record since the patient has left the hospital have never again shown accelerated conduction beats (Figure 3oC)

The sequence of events in this case strongly suggests that the phenomenon of accelerated conduction first appeared after the on et of

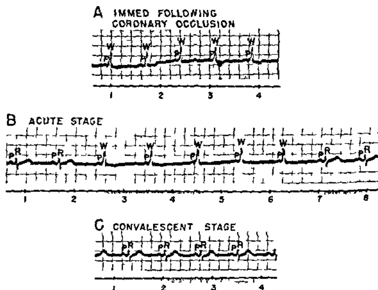


FIG 3o —(A) Continuous accelerated conduction complexes in a patient immediately following posterior wall myocardial infarction Lead 1

(B) A run of accelerated conduction complexes occurring during normal rhythm in the same patient on the day after posterior wall myocardial infarction Lead 1

(C) Disappearance of accelerated conduction during convalescence of same patient with resumption of normal conduction The P R interval now measures 0 14 second Lead 1

Subsequent tracings have shown no accelerated conduction beats during a follow up period of one year

the infarction and as the latter healed the aberration gradually disappeared

CASE 4 This 54 year old man had no evidence of significant heart disease until November 1950 when he suffered an acute posterior wall

myocardial infarction The first electrocardiogram after this episode showed accelerated conduction characterized by short P R interval All subsequent tracings (Figure 36) up to the present have continued to show accelerated conduction

Although there is no proof that this patient did not have accelerated conduction beats before the occurrence of the infarct the unlikelihood

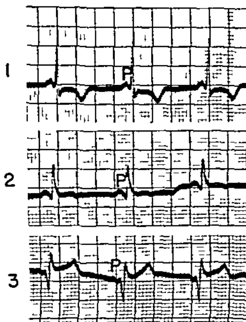


FIG 36—Limb leads showing short P R intervals in a patient with recent posterior wall myocardial infarction

that he had the congenital syndrome and the knowledge that significant cardiac disease was not present prior to the infarction makes it probable that the accelerated conduction beats made their first appearance during the acute phase of the infarction

CASES 5 and 6 These were patients who entered the hospital with typical clinical and electrocardiographic findings of posterior infarction For several days after admission A V conduction was normal Subsequently

however routine tracings showed continuous accelerated conduction beats The further course of these patients is unknown

While the evidence that accelerated conduction in these cases resulted from involvement of the A V node by the posterior myocardial infarctions seem strong histological proof of such involvement is lacking since none of these patients came to autopsy Other similar cases have been brought to our attention by our colleagues

Three Autopsied Cases

Recently we have been fortunate in obtaining autopsy material from three cases with acquired accelerated conduction (Cases 7 8 and 9) Two of these were cases of posterior myocardial infarction with replacement fibrosis of the A V node and bundle of His while the third case of rheumatic heart disease presented a fibrocalcific lesion in the node probably of rheumatic origin

CASE 7 This patient a physician aged 60 had been under our observation for several years During this period repeated electrocardiograms showed P R intervals of normal duration Figure 37A is a reproduction of one of these having a P–R interval of 0 14 second Subsequently the patient developed symptoms characteristic of acute myocardial infarction On the following day the electrocardiogram disclosed evidence of posterior infarction associated with a shortening of the P R interval to 0 10 second indicating accelerated conduction (Figure 37B) During convalescence and for the remaining three years of his life the P R interval invariably measured 0 10 second Follow up physical examinations during this period revealed no evidence of cardiac disease There was no detectable enlargement of the heart and no murmurs could be heard The heart sounds were of good quality and the rhythm remained regular The blood pressure was 125/80 The course of this patient however was progressively downhill due to the intercurrent development of a lymphosarcoma from which he died without evidence of any further cardiac disturbance

At postmortem examination aside from the evidences of lymphosarcoma which were unrelated to the cardiovascular system there was found an old posterior wall myocardial infarct extending into the septum Subsequently because of interest in the A V node and its relation to accelerated conduction a special study was made by Dr Harry Goldblatt and Dr Maurice Lev to determine whether any histological abnormalities of the node and bundle of His could be demonstrated The report of this examination follows

In all parts of the node but especially in the distal portion where it

joins the bundle the amount of fibrous connective tissue and fat is definitely increased [Figure 38] The junctional tissue between node and bundle shows a definite increase in collagen above that of the normal for that age The amount of collagen present in the bundle seems to be in excess for any age and it is interpreted as being a replacement fibrosis The amount of fat in

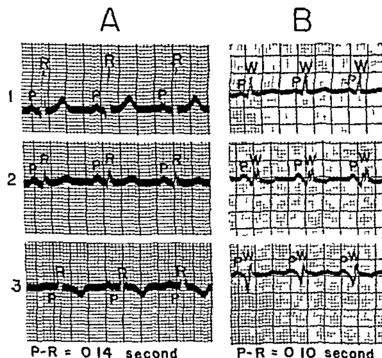


Fig 3(—(A) Normal electrocardiograms of a patient before myocardial infarction The P R interval is within normal limits
(B) Electrocardiogram of same patient one day after posterior wall myocardial infraction The P R interval has become abnormally short and remained so until the death of the patient 3 years later

the proximal part of the node and in other parts of the section in that region although abundant cannot be considered definitely greater than normal for some people after the age of 50 years

CASE 8 This patient a 59 year old man was known to have had essential hypertension for many years During this time repeated electro

inus rhythm no evidence of cardiac enlargement and the blood pressure was 188/92 There was a systolic murmur at the mitral area The second aortic sound was equal to the second pulmonic sound Approximately one year later the patient developed severe coronary artery disease with myocardial infarction About a year after this episode he developed a second posterior wall infarction The electrocardiogram at this time showed a Wenckebach type of heart block as shown in Figure 39B During convalescence this second degree heart block was replaced by first degree heart block This is shown in Figure 39C in which the P R interval measures 0 22 second Some weeks later the P P interval became normal Several months after this tracing however without any new clinical manifestations the electrocardiogram exhibited accelerated conduction with the P R interval measuring 0 09 second (Figure 39D) Subsequently this patient died as a result of a cerebral vascular accident and came to autopsy

The post mortem findings confirmed the diagnosis of a recent extensive cerebral vascular lesion The heart showed evidence of old posterior wall myocardial infarction involving the interventricular septum and caudal region of the right auricle Because of the present investigations the region of the A V node and bundle of His was made the subject of a special study Sections were made by the technique described by Lev [60] The entire block was cut and every 10th section was stained and examined At least 60 slides were examined Every slide showed replacement fibrosis to a significant pathological degree for any age group (Figure 40) The entire region was obviously involved with old infarction Unfortunately in spite of long and careful search the A V node was never positively identified but all the tissues in that region were markedly diseased

It seems probable that in this case the varying state of auriculo ventricular conductivity was dependent upon the varying pathological and physiological conditions prevailing in the A V node and conducting system The changes in A V conduction ranging from heart block to accelerated conduction recall the case described by Levine and Burge [7] in which heart block was interrupted by accelerated conduction complexes (Figure 41) This case would also appear analogous to the experiment illustrated in Figure 21 in which it is shown that electrical alteration of the node can produce accelerated conduction while a more intense disturbance such as excessive pressure results in heart block Thus it would appear that relatively mild alterations in the A V node might give rise to physiological changes permitting accelerated conduction while more severe disturbances in this structure might lead to various degrees of A V block This might provide an explanation for those instances in which both accelerated and decreased nodal conduction (heart block) occur in the same patient

Fig. 40.—Photomicrograph (×50) of region of A-V node from Case 8. There has been extensive replacement fibrosis of this region about the node. The node cannot be recognized. Only small areas of normal tissue (lower right) remain.

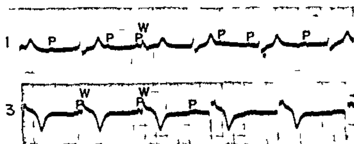


Fig. 41.—Limb leads from a patient who exhibited intermittent runs and single beats of accelerated conduction and also periods of heart block. An isolated accelerated conduction beat is seen in lead 1, while a run of such beats is seen in lead 3. At autopsy a posterior myocardial infarction which involved the A-V node was found. Similar electrocardiograms were recorded when pressure was applied to the A-V node of an animal (see Figure 21).

CASE 9 (Courtesy of Dr Richard Langendorf[51]) This 33 year old woman with rheumatic heart disease was examined in 1945 at which time the electrocardiogram showed regular sinus rhythm a P R interval of 0 11 second and a QRS complex measuring 0 12 second with a slurred upstroke indicating accelerated conduction (Figure 42A) About a year later severe congestive heart failure occurred and the rhythm was found to be totally irregular Tracings at this time revealed auricular fibrillation which under treatment changed to auricular flutter and back again to fibrillation Shortly thereafter the patient developed a pulmonary embolism and died Examination of the A V node was made by Dr Maurice Lev (Figure 42B)

The A V node showed considerable pathologic change This was related to findings in the central fibrous body and the adjacent base of tricuspid and mitral valves These regions and the adjacent ventricular myocardium were markedly calcified The area of calcification compressed the proximal 2/3 of the node the fibers of which were narrow granular and deeply stained In addition there was an increase of connective tissue The distal part of node showed no remarkable changes and retained its connection with the atrial musculature The penetrating portion of the bundle of His showed a slight diffuse increase in connective tissue

The importance of the three autopsied cases cited above is the disclosure of organic histological abnormalities in and about the A V node in patients with accelerated conduction Previously most studies of hearts from patients with accelerated conduction were concerned with the question of the presence or absence of aberrant anatomical auriculo-ventricular connections It is clear that significant pathological changes in the A V node may be overlooked unless this region of the heart is intentionally and carefully examined An excellent technique for this purpose has recently been described by Widran and Lev [60]

It is perhaps premature to assume on the basis of these cases that the short P R interval in instances of the acquired nodal type of accelerated conduction is the result of lesions of the A V node Similar lesions might be found in patients who never display any evidence of accelerated conduction or who develop only heart block Much more clinical and pathological investigation with respect to the A V node is necessary in cases of posterior infarction and other conditions associated with accelerated conduction beats before the nature of the disturbance responsible for the aberration in such cases can finally be established However the finding of a lesion in the node in each of the

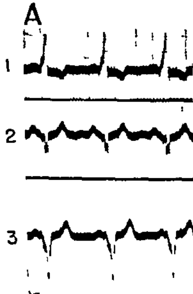




FIG 42 —(A) W I W complexes in a patient with paroxysms of auricular fibrillation and flutter Standard limb leads Autopsy disclosed a calcific lesion of the central fibrous body and adjacent myocardium and base of the tricuspid valve with resulting compression of the proximal 3 of the A V node

(B) Photomicrograph (×50) of region of the A V node of Case 9 An area of calcification compressing the A V node is seen in the lower portion of the figure On one side of the large stained area of calcification there is the node with its fibrosis and its narrow granular muscle fibers

three cases in which it was looked for appears to be more than coincidence. Instances of this kind do not appear to be excessively rare. In addition to the cases reported above we have been apprised of several others of the same kind by colleagues who are aware of our interest in this subject.

It should be pointed out that the presence of accelerated conduction beats may often mask the electrocardiographic characteristic of myocardial infarction and thus render the diagnosis difficult. The appearance of accelerated conduction beats for the first time in a patient who has had an attack of chest pain strongly suggests the development of a posterior myocardial infarct. If infarction involving the A-V node can result in accelerated conduction, it would seem possible that other conditions, for example coronary sclerosis or even inflammatory myocardial disease (as in Case 9), might also produce the same effect if the node were involved by the pathological process. As already indicated, accelerated conduction resulting from any of these causes may be thought of as a relatively mild affection of the A-V node. More advanced lesions of the node will usually produce A-V block of various degrees.

CHAPTER VI

Clinical Significance of Ventricular Type of Accelerated Conduction

ALL THE CLINICAL EXAMPLES of the ventricular type of accelerated conduction appear to be characterized by the presence of a ventricular focus usually associated with ventricular extrasystoles, tachycardia or even paroxysmal ventricular fibrillation.

The first instances of this kind to be considered are those in which accelerated conduction beats occur during catheterization of the heart (Figure 5 and Appendix). In these patients the mechanical stimulation of the ventricle by the catheter is obviously the factor responsible for the appearance of accelerated conduction beats.

A second group of cases probably also representing accelerated conduction of the ventricular type may be distinguished. These are the patients who in addition to having accelerated conduction beats are subject to attacks of paroxysmal ventricular arrhythmias. There is no difficulty in finding such cases among the published instances of paroxysmal ventricular fibrillation. For example, Figure 43 shows the tracings in a case of paroxysmal ventricular tachycardia and fibrillation developing in a patient with a pheochromocytoma following the intravenous administration of Etamon.[49] Figure 43A shows an isolated accelerated conduction beat with a very short P-R interval and deep inversion of the QRS. In Figure 43B the normal complexes alternate with accelerated conduction complexes of the same type as in Figure 43A. At the end of Figure 43C is a short paroxysm of ventricular fibrillation. In figure 43D are seen a few isolated accelerated conduction beats and several ventricular extrasystoles having the same general shape as the accelerated conduction beats. Thus this patient had a ventricular focus as evidenced by the ventricular extrasystoles and fibrillation. When this focus was of somewhat lesser intensity, various types of accelerated conduction beats appeared. In another case

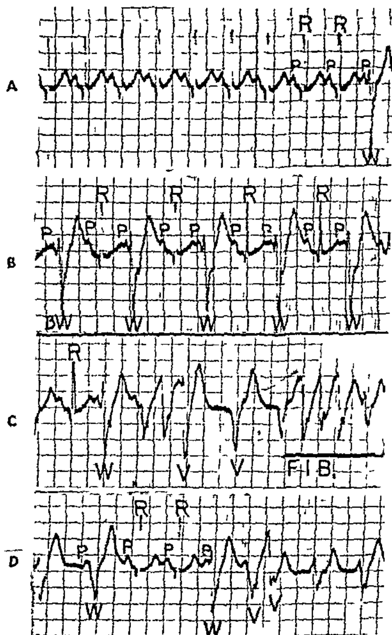


Fig. 43.—Electrocardiogram of a patient with a pheochromocytoma showing the occurrence of accelerated conduction beats W ventricular extrasystoles V and paroxysmal ventricular fibrillation FIB following the intravenous administration of Etamon (tetraethylammonium chloride) Lead 2

described by Schwartz and Jezer[50] there were paroxysms of ventricular fibrillation (Figure 44) and when these attacks subsided the tracings disclosed accelerated conduction beats alternating with normal beats

It has been seen that accelerated conduction beats may result from myocardial infarction involving the A V node Such beats may also occur in patients with myocardial infarction which does not involve

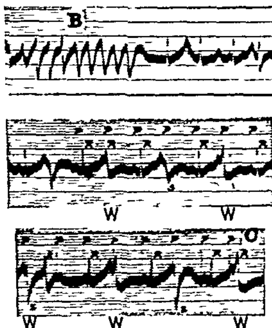


Fig 44—Continuous tracing showing the spontaneous occurrence in a young man of a paroxysm of ventricular fibrillation (B) ventricular extrasystoles (S) and accelerated conduction beats (W) Lead 2

the A V node In our experience the latter cases display ventricular arrhythmias indicating that the aberration is ventricular rather than nodal in origin Figure 45 shows tracings of the onset of short episodes of ventricular tachycardia in a patient shortly after an acute coronary occlusion These paroxysms start with one or two accelerated conduction beats It was possible to record a total of 12 such paroxysms of

which nine were initiated by accelerated conduction beats The similarity to the accelerated conduction beats initiating runs of ventricular tachycardia produced by aconitine (Figure 7) is apparent Figure

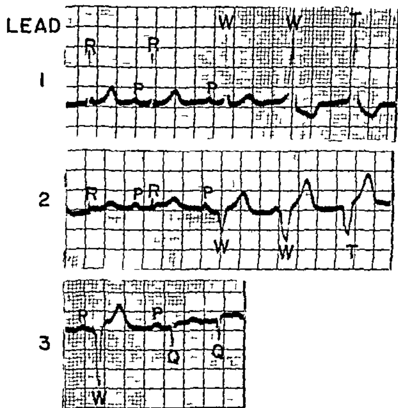


FIG 45 — Patient with recent myocardial infarction showing in leads 1 and 2 the onset of paroxysms of ventricular tachycardia T initiated by accelerated conduction beats W In lead 3 an isolated accelerated conduction beat is shown Note similarity to figure 7 in which paroxysms of ventricular tachycardia initiated by accelerated conduction beats were produced experimentally by chemical stimulation of the ventricle of a dog

46 shows alternating accelerated conduction beats in a dog two days after ligation of a branch of the anterior descending coronary artery The animal later developed attacks of ventricular tachycardia The

association of accelerated conduction and ventricular arrhythmias has been observed in several dogs after the production of anterior wall myocardial infarcts. Thus it seems clear that myocardial infarcts not

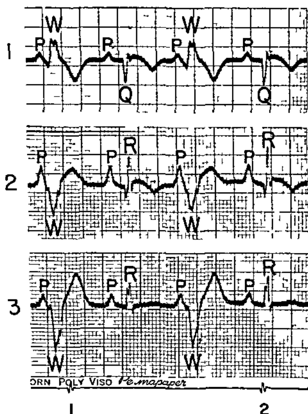


FIG 46.—Standard limb leads of a dog 48 hours after ligation of a branch of the anterior descending coronary artery with resulting anterior wall myocardial infarction showing the occurrence of accelerated conduction beats alternating with normal beats. This aberration persisted for several hours. Ventricular extrasystoles and tachycardia had also occurred in this animal.

involving the A V node can give rise to accelerated conduction. In all probability the aberration in these cases results from irritation of the ventricle by the infarct, perhaps in a manner analogous to the

experimental production of the aberration by mechanical stimulation (Observation 1)

It will be recalled that the experimental production of accelerated conduction beats especially by mechanical and chemical means was frequently accompanied by ventricular tachycardia From a clinical standpoint the converse is also true A careful examination of tracings in instances of paroxysmal ventricular tachycardia will reveal occasional accelerated conduction beats during periods of sinus rhythm in a surprisingly large percentage of cases As seen above accelerated conduction beats also often initiate paroxysms of ventricular tachycardia

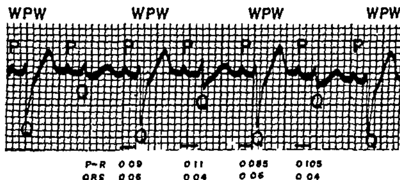


FIG 47 —Accelerated conduction complexes alternating with normal complexes in a dog following the intravenous administration of a large dose of ouabain In this illustration all QRS complexes have been labelled Q

A number of other cases of accelerated conduction have been reported[64] which are probably examples of ventricular tachycardia occurring in association with accelerated conduction beats It is thought by some[51] that these cases are actually instances of auricular fibrillation with very rapid and aberrant ventricular responses While this may be true in many cases it seems probable because of the extremely rapid ventricular rates (as high as 2o0) that some of these cases may be true examples of ventricular tachycardia since it is unlikely that the adult A V node can conduct so rapidly

Accelerated conduction beats which might also be of ventricular origin may *be produced by the administration of certain drugs As long*

ago as *1910* Kahn and Starkenstein[46] noted the appearance of such beats in dogs following the administration of sodium glyoxalate Lindner has observed their occurrence after toxic doses of strophan

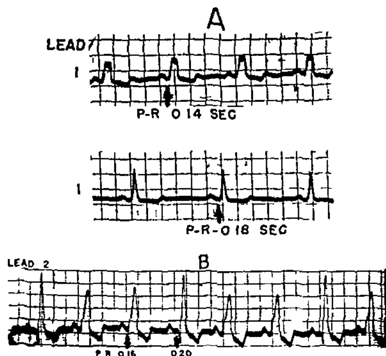


FIG 48 —(A) Lead 1 showing in the upper tracing complexes with relatively short P R intervals and wide aberrant QRS complexes suggesting bundle branch block The lower tracing of the same patient shows return to normal *conduction with longer P R intervals and QRS complexes of normal width* and configuration

(B) Lead 2 from a different patient showing two forms of wide QRS complexes The P R intervals preceding the very wide QRS complexes are shorter than those preceding the narrower QRS complexes

thin[46] Figure 47 shows a run of accelerated conduction beats alternating with normal beats occurring in a dog after the intravenous injection of a large dose of ouabain an observation made in this laboratory by Dr Walter Flieg Accelerated conduction beats have

also been produced in dogs by Stansfield and his associates[65] by the use of 10 per cent tetraethylammonium bromide. Other drugs may also be responsible for the aberration. The method by which these drugs produce accelerated conduction is unknown, but it is postulated that their effect is ventricular, since many of these drugs also produce ventricular tachycardia and extrasystoles.

Finally, there is a small group of cases which probably also represent the ventricular type of accelerated conduction, tracings of which are shown in figure 48. At first these would seem to resemble bundle branch block. It will be noted that the "block" is intermittent and incomplete. With normal ventricular complexes, the P-R intervals are normal, but with the widened ventricular complexes the P-R intervals are slightly shorter. Those beats having short P-R intervals and wide aberrant QRS components probably represent accelerated conduction beats rather than simple bundle branch block, since there is no change in the P-R interval in simple bundle branch block. This type of aberration is probably quite rare.

Discussion

In our limited experience the ventricular types of accelerated conduction are considerably less common clinically than the nodal types. The total number of cases studied to date is small, and more investigation is necessary before accurate classification and analysis of this type of accelerated conduction is possible. The clinical cases representing the ventricular type of accelerated conduction appear to form a heterogeneous group. The reason for bringing together such an apparently diversified collection of cases into one group may be made clearer by pointing out that they all have several features in common.

First, accelerated conduction beats occur in all these cases.

Secondly, there is present a ventricular focus which is responsible for both the accelerated conduction beats and an increased tendency to ventricular extrasystoles and tachycardia, just as in the experimentally produced ventricular type of accelerated conduction. This susceptibility to ventricular rhythms is illustrated by the frequency with which ventricular tachycardia and extrasystoles occur during cardiac catheterization (Figure 5) and by the cases in which these arrhythmias occur spontaneously (Figures 43 and 44). When accelerated conduction beats and ventricular extrasystoles or tachycardia are

associated the QRS complexes of each of these types of aberration are very similar in shape Thus it may be possible to localize the origin of the accelerated conduction beats from the configuration of the extrasystoles or ventricular complexes of the tachycardia

The third feature which all the ventricular types of accelerated conduction have in common is that they are acquired

Fourth in none of the ventricular types of accelerated conduction do supraventricular arrhythmias occur except as an incidental development

In contrast to the situation in acquired nodal accelerated conduction in which the presence of a lesion in the node has been demonstrated by autopsy in three consecutive cases the opportunity to examine the hearts of patients with the ventricular type of accelerated conduction has not yet arisen In such cases however post mortem study is less important because it is obvious from the occurrence of ventricular arrhythmias that a ventricular focus must be present

In the past discussion of accelerated conduction was concerned chiefly with the congenital form of the disorder It was at first rather surprising therefore to be able to find a relatively large number of clinical examples of acquired types of accelerated conduction Now it seems quite probable that the incidence of acquired cases is actually higher than that of the congenital type It is believed that other observers if they will watch for such cases will reach the same conclusion

In terms of the accelerated conduction theory the mechanism of the nodal types of accelerated conduction is relatively clear The function of the A V node is to retard the auricular impulse but in the event of an alteration in the node this function may be impaired and accelerated conduction may result But it is unknown in the ventricular types how a ventricular focus causes accelerated conduction at the A V node As pointed out previously it is possible that antidromic impulses arising from the ventricular focus may affect the A V node in such a fashion that accelerated conduction results in a segmental manner While this explanation is obviously purely speculative it is the best that can be offered with our limited information on this subject

Despite the apparent advantages of the theory of accelerated conduction it must be emphasized that it is still no more than a theory

Most of the work upon which it is based was carried out in dogs and the results obtained are not necessarily valid for the human heart. Furthermore the occurrence of a phenomenon in experimental animals by a given mechanism does not prove that the same mechanism is responsible for the phenomenon in man.

How then may the theory of accelerated conduction be subjected to critical evaluation in man? It does not appear that any single method of testing the theory is applicable to all the different types of accelerated conduction since there is a considerable variation in pathogenesis among the mechanisms. Therefore it is necessary to consider each type individually, for example:

(1) Acquired types of accelerated conduction, such as those resulting from reflex changes or the administration of drugs. In man the aberration produced in these ways is usually transient and of little clinical importance. It is not to be expected that morphologic changes which might explain the mechanism will be found in such cases even if they came to autopsy, and no safe experimental method of testing the theory in man appears available. Thus this type of case does not seem a favorable one for the purpose of testing the theory of accelerated conduction.

(2) Acquired nodal types of accelerated conduction resulting from organic disease. In this group the finding at autopsy of significant lesions in the region of the A-V node, absent in suitable controls, would speak strongly in favor of the theory. It would appear significant that within a brief period, three cases of this kind have been examined post mortem, and in each, a significant lesion has been found in or about the A-V node. Since this type of accelerated conduction is not rare, and since it is often associated with serious organic heart disease, other observers should soon be in a position to study such cases histologically and to provide further information on this subject.

(3) The congenital accelerated conduction syndrome, as originally described by Wolff, Parkinson and White. There are two sets of circumstances which, if they occurred in a patient with the congenital syndrome, would be of great value in testing the theory of accelerated conduction of this type. The first would be a situation in which a patient with the congenital syndrome develops complete heart block later in life as a result of organic disease of the conduction system. In

such an event, if the theory is correct the aberration due to accelerated conduction should be abolished just as it was in Observation 8 where accelerated conduction could not be produced after cutting the bundle of His * Indeed abolition of accelerated conduction is to be expected in all types of the disorder if permanent complete heart block occurs since according to the theory the auricular impulse in accelerated conduction reaches the ventricles only via the bundle of His Proof has already been obtained in this way in cases of ventricular aberration associated with auricular arrhythmias in which it was shown that the ventricular aberration disappeared with the onset of complete heart block

The second circumstance and one which would provide definite proof of the theory would be the discovery of significant pathological changes in the A V node of patients known to have had the congenital accelerated conduction syndrome during life It will be recalled that such evidence has already been demonstrated in three consecutive autopsied cases of *acquired* nodal types of accelerated conduction Such changes should be absent from the hearts of control patients of the same age group The nature of the changes which might be disclosed by histological examination of the node in patient with the congenital syndrome is a matter for speculation It is possible that the lesion in the e cases if it can be demonstrated at all might consist of a subtle alteration of some cells of the node probably in its caudal portion which should be studied with special care The main function of the cells of the A V node is to delay the auricular impulse But since it is not known what histological characteristics correspond with this function it is difficult to know what kind of histological abnormality to seek Nevertheless a careful microscopic examination of the node would be much less laborious than a prolonged search for anomalous A V connections a task which might easily consume several months for a single case The special technique for examination of the A V node described by Widran and Lev [60] is highly recommended Unfortunately we have been unable to find a heart from a patient with the congenital accelerated conduction syndrome It is suggested

Reference has already been made to a single case* in which accelerated conduction beats were interspersed with periods of heart block due to myocardial infarction (Figure 41) This phenomenon was produced experimentally in Observation 5 and is shown in Figure 71

therefore that those who might have the opportunity to examine hearts from such cases or from any of the organic acquired types of this disorder should study the A V node with special care If a significant alteration absent in controls is consistently observed we shall have the solution to a problem which has puzzled cardiologists for many years

For the purpose of clarity the following tentative classification of the numerous and diverse clinical types of accelerated conduction discussed in this paper is offered

(1) *Accelerated Conduction of the Nodal Type*

- (A) Accelerated Conduction Syndrome associated with nodal tachycardia and other supraventricular arrhythmias probably due to congenital abnormality of the A V node This is the Wolff Parkinson White syndrome as originally described and would appear to be the only type that is of congenital origin
- (B) Ventricular aberration occurring with auricular arrhythmias as in auricular premature systoles flutter or fibrillation
- (C) Accelerated conduction beats resulting from involvement of the A V node by posterior myocardial infarction (Cases 3-8) or by other organic disease (Case 9)
- (D) Accelerated conduction beats of probable reflex origin such as those arising from traction on the pulmonary artery etc (Cases 1 and 2)

(2) *Accelerated Conduction of the Ventricular Type*

- (A) Accelerated conduction beats resulting from cardiac catheterization
- (B) Accelerated conduction beats in some patients who develop paroxysms of ventricular tachycardia and fibrillation from *irritable foci in the ventricle*
- (C) Accelerated conduction beats produced by drugs such as digitalis tetraethylammonium chloride etc (Classification as ventricular type uncertain)

Summary and Conclusions

(1) WPW aberration was produced in dogs by continuous sub threshold electrical stimulation of the A V node

(2) WPW aberration was produced in dogs by mechanical chemical and electrical stimulation of the ventricles and occurs in man as a result of endocardial stimulation of the ventricles during cardiac catheterization

(3) Thus two experimental types of WPW aberration may be distinguished (a) nodal type having its origin in the A V node and (b) ventricular type having its origin in the ventricles

(4) By these methods all the recognized clinical variations of WPW aberration were produced These include isolated WPW beats continuous WPW aberration WPW complexes alternating with normal complexes the concertina effect WPW aberration of very minor degree and WPW complexes with QRS components of various configurations

(5) When the area in the A V node which is responsible for the nodal type of WPW aberration becomes the pacemaker paroxysmal tachycardia and other supraventricular arrhythmias result Thus the entire clinical WPW syndrome may be reproduced by modifying the A V node

(6) The theory of anomalous anatomical A V bundles offers an explanation for the occurrence of auricular tachycardia in the WPW syndrome by assuming retrograde ventriculo auricular conduction However it cannot explain by this mechanism the occurrence of flutter and fibrillation since impossibly rapid rates of ventricular contraction would be required All these supraventricular arrhythmias were produced in the present investigation by making the A V node the pacemaker Hence their clinical occurrence in the WPW syndrome may be explained by the assumption by the A V node of the role of a rapidly discharging pacemaker

(7) WPW aberration depends upon the presence of an intact normal conduction system and not upon the presence of anomalous anatomical A V pathways since (a) When the bundle of His was cut WPW aberration could not be produced (b) the ventricular type of WPW aberration resulted from stimulating the ventricles at points far removed from any known anomalous anatomical pathways (c) the aberration can be produced in practically all dogs and in human patients It cannot be assumed that all these subjects have accessory conduction systems which suddenly become functional

(8) By means of a new technique utilizing high speed cinematography of the motions of the ventricles and simultaneous electrocardiograms as they were being written the details of ventricular movements in WPW aberration were studied and correlated with their corresponding electrocardiographic events This method yielded the information that the kinetics of a usual WPW beat may consist of four phases

(a) premature contraction of a limited area of one ventricle
(b) contraction of the remainder of the ventricles (through the normal mechanism)
(c) diastolic relaxation and protrusion of the prematurely contracted area while the remaining parts of the ventricle are still contracted
(d) relaxation of the rest of the ventricles

The premature contraction is weak and does not expel blood from the ventricle The diastolic protrusion of this area is often very striking and clearly delineates its location and extent

(9) Detailed correlation of these kinetic events with the electrocardiographic phenomena occurring simultaneously demonstrates that the early slurred R wave is associated with the premature localized contraction and that the rest of the R wave may be correlated with the normal contraction of the remainder of the ventricular musculature The ST and T components of the complex are the result of the combined repolarization effects following the two contractions The WPW complex as a whole is thus seen to be a fusion complex composed of a premature localized contraction in one ventricle and the normal contraction of the rest of the ventricular musculature

(10) The differences which occur in various forms of WPW complexes may be explained by two factors the location of the prema

turely contracting area and the degree of prematurity of its contraction In the two cinematographic experiments in which accelerated conduction was produced by stimulating the A V node the P R intervals were short and the ventricular motions and QRS complexes were normal

(11) The above observations can explain various clinical forms of WPW aberration and show how the QRS component may assume practically any configuration

(12) The term *accelerated conduction* is introduced to describe the physiological process which accounts for the premature transmission of the excitation wave from the auricles to part of one ventricle in WPW aberration The term *accelerated conduction syndrome* is suggested to describe the congenital syndrome as described by Wolff Parkinson and White The term *accelerated conduction beat* may be used to describe individual beats in all forms of accelerated conduction whether congenital or acquired

(13) The theory of accelerated conduction is attractive since (a) normally there is a delay of the excitation wave at the A V node (b) in WPW aberration some of this delay is absent at part of the A V node while the rest of the node delays its share of the impulse in a normal manner (c) both the accelerated and normally delayed impulses pass down the bundle of His (d) the node and bundle of His seem to be constituted so that a given area of the node always supplies the same area of the ventricular myocardium

(14) There are two types of clinical accelerated conduction the nodal and the ventricular These are analogous to the experimental nodal and ventricular types

(15) The most important example of the nodal type is the congenital accelerated conduction syndrome Other examples are the ventricular aberration which may occur with auricular arrhythmias and the accelerated conduction due to reflex mechanisms such as may result from traction on the pulmonary artery

(16) Also of the nodal type are the six cases reported in this paper in which accelerated conduction resulted from involvement of the A V node by posterior myocardial infarction In these cases it is postulated that ischemic changes in the node were responsible for the appearance of accelerated conduction

(17) All the clinical examples of the ventricular type of accelerated

conduction are characterized by the presence of an irritable ventricular focus The conditions comprising this group include cases developing accelerated conduction during cardiac catheterization probably some cases of apparent partial or intermittent bundle branch block instances of accelerated conduction following the administration of certain drugs such as digitalis and tetraethylammonium chloride (etamon) and a group of cases which develop in addition to accelerated conduction beats other evidences of irritable ventricular foci such as ventricular extrasystoles paroxysmal ventricular tachycardia or occasionally even paroxysmal ventricular fibrillation

(18) The incidence of clinical cases of acquired forms of accelerated conduction appears to be greater than that of the congenital form

(19) *Strong evidence in favor of the accelerated conduction theory* would be obtained if patients with accelerated conduction either congenital or acquired were found to lose the aberration after the onset of complete heart block

(20) Further proof of the theory would be at hand if in nodal type of accelerated conduction significant lesions absent in suitable controls were consistently found in the AV node It is suggested that careful histological examination of this region be made in all cases of nodal accelerated conduction whether congenital or acquired

(21) Of 3 consecutive cases of acquired nodal accelerated conduction which have come to autopsy significant lesions in and about the AV node were found in each In 2 of these which were due to posterior wall myocardial infarcts replacement fibrosis of the node and bundle was found In the third case a calcified lesion probably of rheumatic origin was found in the node

Appendix

Relative Incidence of WPW Complexes and Ventricular Premature Systoles Produced by Ventricular Stimulation—A Statistical Analysis of Observations 1 and 2

IN THE EXPERIMENTS described above WPW complexes were produced in dogs by several variations of two main types of stimuli, mechanical (tactile) and chemical. WPW complexes were also observed to occur in a limited number of patients during the course of cardiac catheterization studies. However, in both the animal and human observations ventricular premature systoles frequently appeared in addition to the WPW complexes.

Since both phenomena were produced and since the production of one or the other depends upon the time during the non-refractory period of the cardiac cycle at which a premature ventricular discharge occurs, the possibility arises that the WPW complexes appeared as a result of chance. This question may be examined by a statistical analysis as follows.

A premature ventricular response which occurs during the interval between the crest of a P wave and the onset of the QRS will produce a WPW complex. This period usually occupies about 20 per cent of the non-refractory period at the cardiac rates encountered clinically and in these experiments. On the other hand, a premature ventricular response occurring at any other point in the non-refractory period will produce a premature ventricular systole. The portion of the non-refractory period during which this phenomenon is possible extends from the end of the refractory period to the crest of the P wave and comprises about 80 per cent of the total non-refractory period. If, therefore, the appearance of WPW complexes or ventricular premature systoles in these experiments were governed by the law of chance, stimulation of the ventricles at random times during the cardiac cycle should produce WPW complexes and ventricular pre

mature systoles in a numerical ratio of approximately 20 to 80. The abnormal ventricular complexes recorded during the experiments were counted as follows. Each WPW complex preceded and followed by a normal ventricular complex was counted as one WPW. Each isolated ventricular premature systole was counted as one VPS. Runs of ventricular tachycardia starting with a premature systole were counted as one VPS. Runs of WPW complexes were counted as one WPW. Over 50 per cent of the runs of ventricular tachycardia started with one or more WPW complexes; these were counted as one WPW. A similar method was used to determine the relative incidence of WPW complexes and ventricular premature systoles produced by intracardiac catheterization in a small series of patients. As shown in the table, the observed ratio in both human and animal studies was significantly different from the ratio predicted on the basis of the law of chance. If accurate counts of sufficient numbers of these two types of complexes obtained experimentally by ventricular stimulation at random times during the cardiac cycle result in a ratio significantly higher than 20 to 80, the possibility of the chance occurrence of WPW complexes tend to be excluded. Stated conversely, the probability that the production of WPW complexes in these experiments represents a fundamental physiologic phenomenon increases.

Applying this method to the observations made during catheterization studies in human subjects and in the experiments already described, the following results were obtained:

	Method of Stimulation	
	Mechanical and Chemical (dogs)	Catheterization (man)
Average heart rate	130 per minute	80 per minute
Total number of abnormal responses (WPW + VPS)	1231	191
Predicted ratio on basis of chance — WPW / VPS	213 (20%) / 994 (80%)	38 (20%) / 153 (80%)
Observed ratio — WPW / VPS	601 (48%) / 642 (52%)	84 (44%) / 107 (56%)

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Index